

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<u>http://bmjopen.bmj.com</u>).

If you have any questions on BMJ Open's open peer review process please email <u>info.bmjopen@bmj.com</u>

BMJ Open

Efficacy of low-level laser therapy in patients with lower extremity tendinopathy or plantar fasciitis: systematic review and meta-analysis of randomised controlled trials

Journal:	BMJ Open
Manuscript ID	bmjopen-2021-059479
Article Type:	Original research
Date Submitted by the Author:	21-Nov-2021
Complete List of Authors:	Naterstad, Ingvill; University of Bergen, Department of Global Public Health and Primary Care Joensen, Jon; University of Bergen, Department of Global Public Health and Primary Care Bjordal, Jan; University of Bergen, Department of Global Public Health and Primary Care Couppe, C; Bispebjerg Hospital, Institute of Sports Medicine Copenhagen Lopes-Martins, Rodrigo; Universidade do Vale do Paraíba, Instituto de Pesquisa & Desenvolvimento Stausholm, Martin; University of Bergen, Department of Global Public Health and Primary Care
Keywords:	Laser therapy < DERMATOLOGY, GENERAL MEDICINE (see Internal Medicine), REHABILITATION MEDICINE





I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

terez oni

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies



Efficacy of low-level laser therapy in patients with lower extremity tendinopathy or plantar fasciitis: systematic review and meta-analysis of randomised controlled trials

Ingvill Fjell Naterstad¹, Jon Joensen¹, Jan Magnus Bjordal¹, Christian Couppé^{2,3}, Rodrigo Alvaro Brandão Lopes-Martins⁴, Martin Bjørn Stausholm¹

¹Department of Global Public Health and Primary Care, University of Bergen, Bergen, Norway ²Institute of Sports Medicine Copenhagen, Bispebjerg Hospital, Copenhagen, Denmark ³Center for Healthy Aging, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

⁴Post-Gradute Program in Pharmacology, Faculty of Medical Sciences, State University of Campinas, Sao Paolo, Brazil

Correspondence to: Ingvill Fjell Naterstad naterstad@gmail.com

Word count: 4550

Abstract

Objectives We investigated the effectiveness of low-level laser therapy (LLLT) in lower extremity tendinopathy and plantar fasciitis on patient-reported pain and disability.

Design Systematic review and meta-analysis.

Data sources Eligible articles in any language were identified through PubMed, Embase and Physiotherapy Evidence Database (PEDro) on the 20th August 2020, references, citations and experts.

Eligibility criteria for selection of studies Only randomised controlled trials involving participants with lower extremity tendinopathy or plantar fasciitis treated with LLLT were included.

Data extraction and synthesis Random effects meta-analyses with dose subgroups based on the
 World Association for Laser Therapy (WALT) recommendations were conducted. Risk-of-bias was assessed with the PEDro scale.

Results LLLT was compared with placebo (10 trials), other interventions (5 trials) and as an add-on intervention (3 trials). The study quality was moderate-high.

Overall, pain was significantly reduced by LLLT at completed therapy (13.15 mm Visual Analogue Scale (VAS; 95% CI: 7.83-18.48)) and 4-12 weeks later (12.56 mm VAS (95% CI: 5.69-19.42)). Overall, disability was significantly reduced by LLLT at completed therapy (Standardised Mean Difference (SMD) = 0.39 (95% CI: 0.09-0.7) and 4-9 weeks later (SMD = 0.32 (95% CI: 0.05-0.59)). Compared with placebo-control, the recommended doses significantly reduced pain at completed therapy (14.98 VAS mm (95% CI: 3.74-26.22)) and 4-8 weeks later (14.00 mm VAS (95% CI: 2.81-25.19)). The recommended doses significantly reduced pain as an add-on to exercise therapy versus exercise therapy alone at completed therapy (18.15 mm VAS (95% CI: 10.55-25.76)) and 4-9 weeks later (15.90 mm VAS (95% CI: 2.3-29.51)). No adverse events were reported.

Conclusion LLLT reduces pain in lower extremity tendinopathy and plantar fasciitis compared with placebo, other treatments and as a supplement to exercise therapy. LLLT reduces disability to a small extent in the patients. Adhering to the WALT recommendations is advised. **PROSPERO registration number** CRD42017077511

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

5

6 7 8

9

10

11

12

13

14

15

16 17

18

19 20

21

22

23

24 25

26

27

28

29

30

31 32

33

34

35

36

37

38

39 40

41

42

43

44

45

46 47

48 49

50

51

52

53

54 55

56

57

58

59 60 Keywords Phototherapy; Laser therapy; Tendinopathy; Plantar Fasciitis; Systematic review; Metaanalysis

Strengths and limitations of this study

- ► This review was performed in conformance with a prospective published protocol, which included a plan for subgrouping the trials by laser dose.
- ► There were no language restrictions; two (11%) of the included trials were reported in non-English language.
- ► The review includes results from an unpublished trial.
- ► The review features meta-analyses with direct comparisons between low-level laser therapy and placebo, other interventions and no intervention.
- Only one reviewer extracted data from the included trials, but the extracted data was checked for correctness by another reviewer.

INTRODUCTION

Tendinopathy and plantar fasciitis are common disorders resulting in substantial pain and loss of function in the lower extremity, and both disorders are especially prevalent in athletic and non-athletic populations.¹⁻³ The aetiology of tendinopathy and plantar fasciitis is multifactorial, and not fully understood. Risk factors for tendinopathy include overuse, acute trauma, ageing and genetic predisposition^{4 5}, while prolonged standing and jumping, reduced ankle dorsiflexion and obesity are known risk factors for plantar fasciitis.⁶⁻⁹ Disorganised and degenerating collagen fibres, increased numbers of fibroblasts, altered composition of extracellular matrix proteins, formation of new vessels and rounding of tendon cells can be found in both tendinopathy and plantar fasciitis.^{10 11}

Conservative treatment of lower extremity tendinopathy and plantar fasciitis includes an array of modalities and approaches. The effect of exercise therapy in tendinopathy is wellestablished, and any exercise type is preferential to wait-and-see in the earlier stages of tendinopathy.¹² However, a superiority of exercise therapy compared with other interventions has not been demonstrated. The use of non-steroidal anti-inflammatory drugs (NSAIDs) are frequently recommended in the early stages of tendinopathy and plantar fasciitis.¹³⁻¹⁵ However, there is a lack of placebo-controlled trials investigating the effectiveness of NSAIDs in lower extremity tendinopathies.¹⁶⁻²⁰ Moreover, NSAIDs have well known and potentially fatal side-effects, most importantly severe cardiovascular events and gastrointestinal toxicity.²¹ Low-level laser therapy (LLLT), also known as photobiomodulation therapy, is a quickly administered non-invasive intervention option free from negative side-effects. LLLT is an athermic photochemical modality, where red or near-infrared light is used to stimulate tissue healing, reduce pain and inflammation.²²⁻ ²⁵ The working mechanisms of LLLT are partly established. There is evidence that LLLT increases adenosine triphosphate production²⁶, modulates the reactive oxygen species and the induction of transcription factors.²⁷⁻³⁰ Besides, it has been demonstrated that LLLT inhibits cyclooxygenase-2 gene expression and prostaglandin E2 production in tendons^{31 32}, as well as inhibition of matrix metalloproteinase activity.^{32 33} Furthermore, under application of LLLT, macrophages are more likely to act as phagocytes.³⁴

There are heterogeneous results from clinical trials of LLLT in tendinopathies, and this may or may not be explained by a dose-response relationship.³⁵⁻³⁷ Variation in LLLT parameters, such as wavelength, power density, pulse structure, application method and timing may affect the treatment outcome. Additionally, several in vivo and in vitro trials have demonstrated that when the LLLT dose is increased beyond a certain level, the response diminishes.³⁸⁻⁴¹ In a recent review by our research group regarding the effectiveness of LLLT in knee osteoarthritis, a significant doseresponse relationship was discovered when the included trials were subgrouped using the World Association for Laser Therapy (WALT) treatment recommendations.⁴² Several recent systematic reviews have either solely focused on LLLT or included the modality as one of several conservative treatments in Achilles tendinopathy or plantar fasciitis.^{12 43-48} Unfortunately, these reviews have one or more substantial limitations, such as a lack of a dose-response analysis¹², a lack of inclusion of trials reported in non-English languages⁴³⁻⁴⁷, or the faulty use of a fixed effects meta-analysis model in the presence of highly heterogeneous studies⁴⁸.

Thus, the potential benefits of managing pain and disability associated with lower limb tendinopathy and plantar fasciitis have been investigated using LLLT but are still somewhat inconclusive. Further explorations into the clinical effectiveness of LLLT are warranted, and the objective of the current review were hence to estimate the effectiveness of LLLT in tendinopathy and plantar fasciitis on patient-reported pain and disability with a dose-response analysis.

METHODS

 This review adheres to a prospectively registered PROSPERO protocol and is reported in accordance with the Preferred Reporting Items of Systematic reviews and Meta-Analysis statement 2009.⁴⁹

Literature search and selection of studies

We included randomised clinical trials in which the effectiveness of LLLT in tendon disorders of the lower extremity or plantar fasciitis was compared with sham (placebo) LLLT, other interventions or no intervention, in terms of self-reported pain and/or disability. There were no restrictions regarding publication date and language.

An updated search of the databases PubMed, Embase and Physiotherapy Evidence Database (PEDro) was completed on the 20th August 2020. Furthermore, references from relevant systematic reviews^{44 46 48 50 51} and all the included trials were screened, and experts in the field were asked to provide additional published and unpublished trials. Abstracts were not included. The full electronic search strategy is included in the supplementary material.

Two independent reviewers (IFN and MBS) read the titles and abstracts of the publications identified by the search. Any article judged potentially eligible by a reviewer was retrieved in full text. The same two reviewers evaluated the full texts of all the potentially eligible articles and made a careful decision to include or exclude each article, with close attention to the eligibility criteria. Any article not fulfilling the eligibility criteria was excluded and had its details listed with reason for exclusion (supplementary material). Selection disagreements were resolved by discussion to consensus with the option of a third person's (JJ) final decision if necessary.

Risk-of-bias analysis

Two reviewers (IFN and MBS) independently assessed the risk-of-bias of the included trials with the 0-10 points PEDro scale.⁵² This was done on outcome level, and since the outcomes of interest are patient-assessed pain and disability, the participants were considered the assessors. Therefore, the assessors can only be blinded in placebo-controlled trials. When risk of bias disagreements could not be resolved by discussion, a third reviewer (JJ) made the final consensus-based decision. The trials were labelled as being of 'high', 'moderate' or 'poor' methodological quality if they had a total PEDro score of \geq 7, 5-6 and \leq 4, respectively.⁵³ Risk of publication bias was assessed with a funnel plot.

Data-extraction and meta-analysis

Extraction of the following information was mandatory: number of participants allocated to laser and control groups, participant characteristics, type and duration of interventions, laser-specific

BMJ Open

application information (including location of application, wavelength, energy density per treated spot, number of spots treated, mean power density per treated spot, treatment time per spot, treated area and total number of laser sessions and laser sessions per week), selected outcome measurement scales for data-extraction, time-points of assessments, effect estimates and adverse events.

The data collection was handled in a two-person procedure by IFN and MBS. Initially, one reviewer entered all the data in Excel sheets and then another reviewer checked the extracted data for correctness. If data-extraction disagreements could not be resolved by discussion, a third reviewer (JMB) made the final consensus-based decision.

All meta-analyses were conducted using random effects models, weighting the individual trial results relatively even when statistical heterogeneity is present.

Pain results were synthesised using the Mean Difference (MD) method as this method allows for change and final scores to be combined.⁵⁴ Pain scores reported on the Visual Analogue Scale (VAS) and on the Numeric Rating Scale highly correlates⁵⁵ and were thus considered the same. Self-reported disability results were synthesised with the Standardised Mean Difference (SMD) method using change scores solely.⁵⁴ According to Cohen, a SMD of 0.2, 0.5 and 0.8 can be considered small, moderate and large, respectively.⁵⁴

Heterogeneity was measured using I²-statistics (inconsistency).⁵⁶ An inconsistency level of 25%, 50% and 75% would be considered low, moderate and high, respectively.⁵⁷ Standard deviations (SD) for meta-analysis were extracted or estimated from other variance data in the following prioritised order: SD, standard error, 95 % confidence interval, p-value, interquartile range, median of correlations, visually from graph, correlation of 0.6 or mean of SDs from similar trials.

Trials were subgrouped by laser dose using the World Association of Laser Therapy (WALT) treatment recommendations^{58 59}, as specified in the a priori protocol. WALT recommends irradiating minimum of 2-3 points on the tendon or fascia. In Achilles and patellar tendinopathy, the recommended dose with 904 nanometer (nm) wavelength laser is minimum 2 Joules per point. Utilizing 780-860 nm wavelength laser, the minimum dose is 4 Joules per point. In plantar fasciitis, the recommended minimum dose is 2 Joules per point with a 904 nm laser or 4 Joules per point with 780-860 nm laser. We subgrouped the trials as recommended dose and non-recommended laser dose. If the trial reports lacked sufficient dose parameters to be identified as recommended or non-recommended dose, they were subgrouped as unknown dose.

Two time-points of assessment were selected for analysis, that is, immediately after the end of LLLT and last time-point of assessment 2-14 weeks after completed LLLT (follow-up).

IFN and MBS performed the meta-analyses, using Excel 2016 (Microsoft) and Review Manager Version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014).

Patient and public involvement

Patients or the public were not involved in the conceptualization or carrying out of this research.

RESULTS

A total of 870 publications were identified in the search, of which 18 trials (N = 784) were included in review and meta-analysis (Figure 1 and Table 1). LLLT was applied to participants with patellar tendinopathy in 2 trials, Achilles tendinopathy in 5 trials, and plantar fasciitis in 11 trials. LLLT was compared with placebo (10 trials), other interventions (5 trials) and as an adjunct intervention (3 trials). Two trials were reported in non-English language, and one trial was unpublished. The excluded articles were listed with reasons for omission (supplementary material). The mean age of the participants was 43.6 (minimum <18, maximum 54.5, data from 14 trials), and the mean

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

baseline pain intensity was 64.2 mm on the VAS (minimum 19.3 mm, maximum 85 mm, data from 18 trials). No adverse events were reported by any of the trial authors. None of the trial authors declared that they had received funding from the laser industry.

Figure 1 Flow chart illustrating the trial identification process PEDro, Physiotherapy Evidence Database.

First author, year	Participants at baseline (intervention)*	Participants at baseline (control)*	Intervention versus control	Outcome and time of reassessment after baseline (time used for analysis in bold
Patellar tendinopat		. ,		· ·
Liu 2014 ⁶⁰ , LLLT versus ET	N: 7 Age years: \geq 18, \leq 23 VAS Pain mm: 67.86	N: 7 Age years: ≥ 18, ≤ 23 VAS Pain mm: 65,71	4 weeks of LLLT versus 4 weeks of eccentric ET	Pain: VAS Disability: Modified-VISA Reassessment: 4 weeks
Liu 2014 ⁶⁰ , LLLT+ET versus ET	N: 7 Age years: ≥ 18 , ≤ 23 VAS Pain mm: 67.86	N: 7 Age years: ≥ 18, ≤ 23 VAS Pain mm: 65.71	4 weeks of LLLT and eccentric exercise therapy versus 4 weeks of eccentric ET	Pain: VAS Disability: Modified-VISA Reassessment: 4 weeks
Stergioulas 2003 ⁶¹	N: 23 Age years: 29.2 VAS Pain mm: 81.7	N: 21 Age years: 29.8 VAS Pain mm: 75.9	2 weeks of LLLT versus 2 weeks of sham LLLT	Pain: VAS Disability: Functional Index Questionnaire Reassessment: 2 and 6 weeks
Achilles tendinopat	hy			
Darre 1994 ⁶²	N: 46 Age years: ≥ 18 VAS Pain mm: 58.5	N: 43 Age years: ≥ 18 VAS Pain mm: 72	2.4 weeks of LLLT versus 2.4 weeks of sham LLLT	Pain: VAS Disability: - Reassessment: 2.4 weeks
Naterstad ⁶³ (unpublished)	N: 20 Age years: 45.4 VAS Pain mm: 52.9	N: 21 Age years: 45.8 VAS Pain mm: 53.8	4 weeks of LLLT and cryotherapy and 12 weeks of eccentric and concentric ET versus 4 weeks of sham LLLT and cryotherapy and 2 weeks of eccentric and concentric ET	Pain: THIP VAS most painful activity Disability: THIP VAS ADL Reassessment: 4 and 12 weeks
Stergioulas 200864	N: 20 Age years: 30.1 VAS Pain mm: 79.8	N: 20 Age years: 28.8 VAS Pain mm: 81.8	8 weeks of LLLT and eccentric ET versus 8 weeks of sham LLLT and eccentric ET	Pain: VAS during activity Disability: - Reassessment: 4, 8 and 12 weeks
Tumilty 200865	N: 10 Age years: 41.4 VAS Pain mm: 47.8	N: 10 Age years: 42.5 VAS Pain mm: 39	4 weeks of LLLT and 12 weeks of eccentric ET versus 4 weeks of sham LLLT and 12 weeks of eccentric ET	Pain: VAS in morning Disability: - Reassessment: 4 and 12 weeks
Tumilty 201266	N: 20 Age years: 45.6 NRS Pain mm: 21.1	N: 20 Age years: 46.5 NRS Pain mm: 19.3	4 weeks of LLLT and 12 weeks of eccentric ET versus 4 weeks of sham LLLT and 12 weeks of eccentric ET	Pain: NRS Disability: - Reassessment: 4 , 12 and 52 weeks
Plantar fasciitis				
Basford 1998 ⁶⁷	N: 16 Age years: 42.5 VAS Pain mm: 46.6	N: 15 Age years: 42 VAS Pain mm: 57.9	4 weeks of LLLT versus 4 weeks of sham LLLT	Pain: Pain when walking in morning Disability: Limping in morning Reassessment: 2, 4 and 8 weeks
Cinar 2017 ⁶⁸	N: 29 Age years: 46.59 VAS Pain mm: 61.3	N: 22 Age years: 44.18 VAS Pain mm: 54.9	3 weeks of LLLT and stretching versus 3 weeks of stretching	Pain: VAS Disability: AOFAS-F activity limitations Reassessment: 3 and 12 weeks
Cinar 2018 ⁶⁹	N: 24 Age years: 46.5	N: 17 Age years: 44 NRS Pain mm: 62	3 weeks of LLLT and 12 weeks of stretching versus 12 weeks of stretching	Pain: NRS Disability: - Reassessment: 3 and 12 weeks

	NRS Pain mm:			
	63			
Cinar 201869,	N: 24	N: 25	3 weeks of LLLT and 12 weeks of	Pain: NRS
ESWT	Age years: 46.5	Age years: 45.4	stretching versus 3 weeks of ESWT (2000	Disability: -
	NRS Pain mm:	NRS Pain mm: 67	mJ/mm ² , session once per week) and 12	Reassessment: 3 and 12 week
	63		weeks of stretching	
Elsehrawy 201870	N: 23	N:23	3 weeks of LLLT versus 2 weeks of ESWT	Pain: VAS
	Age years: 46.4	Age years: 46	(2050 shocks/min, 10 Hz, 2.5 bars once per	Disability: FFI disability
	VAS pain: 85	VAS pain: 82	week)	subscale
				Reassessment: 4 weeks
Kiritsi 201071	N: 15	N: 15	6 weeks of LLLT versus 6 weeks of sham	Pain: ADL VAS
	Age years: 41	Age years: 41	LLLT	Disability: -
	VAS Pain mm:	VAS Pain mm: 67		Reassessment: 6 weeks
	67			
Koteeswaran	N: 15	N: 15	2 weeks of LLLT and stretching versus 2	Pain: NRS
202072	Age years: 30-	Age years: 30-60	weeks of TUS and stretching	Disability: FAAM
	60	NRS Pain: 72.7		Reassessment: 2 weeks
1 201273	NRS Pain: 74.7	N. 40		
Lamba 201373	N: 40	N: 40	4 weeks of LLLT and stretching versus 4	Pain: VAS
	Age years: 40.9 VAS Pain mm:	Age years: 40.4 VAS Pain mm: 62	weeks of sham LLLT and stretching	Disability: -
	VAS Pain mm: 57.5	VAS Pain mm: 62		Reassessment: 1,2, 3 and 4 weeks
Macias 201574	N: 37	N: 32	3 weeks of LLLT versus 3 weeks of sham	Pain: VAS heel pain
Macias 2015	Age years: ≥ 18	Age years: ≥ 18	LLLT	Disability: FFI disability
	VAS Pain mm:	VAS Pain mm:		subscale 8 weeks
	69.1	67.6		Reassessment: 1, 2, 3, 6 and
	07.1	07.0		weeks
Sanmak 201975	N: 17	N: 17	4 weeks of LLLT versus 3 weeks of ESWT	Pain: VAS
	Age years: 53	Age years: 49	(2 bar with 2,000 shocks/min at 10 Hz once	Reassessment: 4 and 8 week
	VAS Pain mm:	VAS Pain mm: 80	per week)	
	70			
Ulusoy 201776,	N: 20	N: 20	3 weeks of LLLT versus 3 weeks of TUS (1	Pain: VAS in morning
TUS	Age years: 53.4	Age years: 50.95	mHz; 2 W/cm2)	Disability: -
	VAS Pain mm:	VAS Pain mm:		Reassessment: 7 weeks
	68.7	66.6		
Ulusoy 201776,	N: 20	N: 20	3 weeks of LLLT versus 3 weeks of ESWT	Pain: VAS in morning
ESWT	Age years: 53.4	Age years: 54.45	(2.5 bar with 2,000 shocks/min at 10 Hz	Disability: -
	VAS Pain mm:	VAS Pain mm: 66	three times per week)	Reassessment: 7 weeks
	68.7			
Yüzer 200677	N: 24	N: 30	1.4 weeks of LLLT versus steroid injection	Pain: VAS
	Age years: 49.58	Age years: 51.53		Disability: -
	VAS Pain mm:	VAS Pain mm: 76		Reassessment: 5.4, 13.4 and
	80			25.4 weeks

ADL, activity of daily living; AOFAS-F, American Orthopedic Foot and Ankle Score Function; ESWT, Extracorporeal Shockwave Therapy; ET, exercise therapy; FAAM, Foot and ankle ability measurement questionnaire; FFI, Foot Function Index; LLLT, Low-Level Laser Therapy; NRS, Numeric Rating Scale; THIP, Tendinopathy Health Impact Profile; TUS, therapeutic ultrasound; VAS, Visual Analogue Scale.

LLLT was compared with placebo LLLT in 10 trials^{61-63 65-67 71 73 74 78}, and exercise therapy or stretching exercises was applied as a co-intervention in five of these trials. LLLT was compared with exercise therapy or stretching exercises in three trials.^{60 68 69} A comparison between LLLT and Extracorporeal Shockwave Therapy (ESWT) in plantar fasciitis was performed in four trials.^{69 70 75} ⁷⁶ LLLT was compared to therapeutic ultrasound in two trials^{72 76}, and LLLT was compared to steroid injection in one trial⁷⁷. Recommended laser doses were applied in at least 11 trials^{60-65 68 69 71} ^{73 76} and a non-recommended dose was used in at least one trial.⁶⁶ We were unable to categorise the laser doses in the remaining six trials^{67 70 72 74 75 77} due to inadequately or missing descriptions of laser parameters (Table 2).

60

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

2
3
4
5
6
7
, 8
9
10
11
12
13
14
15
16 17
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
40
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
58 59
60

First author, year	Wave- length (nm)	Mean output power (mW)	Seconds per treatment spot (s)	Joules per treatment spot (J)	Number of spots treated	Number of sessions/Weeks	Dose recommended by WALT
Patellar tendinopathy							
Liu 201460	810	200	600	-	1	24/4	Yes
	810	200	300	-	2*		
Stergioulas 200361	904	50	300	1.2	10	10/2	Yes
Achilles tendinopathy							
Darre 199462	830	30	-	4	4	12/2.5	Yes
Naterstad63 (unpublished)	904	60	50	3	6	12/4	Yes
Stergioulas 200864	820	30	-	0.9	6	12/8	Yes
Tumilty 200865	810	100	30	3	6	12/4	Yes
Tumilty 201266	810	7	30	0.21	6	12/4	No
Plantar fasciitis							
Basford 199867	830	30	-	-	3 *	12/4	Unclear
Cinar 201768	830	100	80	5.6	5	10/3	Yes
Cinar 201869	830	100	80	5.6	5	10/3	Yes
Elsehrawy 201870	830	-	-	-	3 *	6/3	Unclear
Kiritsi 201071	904	60	-	8.4	1	18/6	Yes
	904	60	-	-	2 *		
Koteeswaran 202072	830		180	-	3	9/3	Unclear
Lamba 201373	820	100	80	-	3 *	12/4	Yes
Macias 201574	635	17	600	-	3	6/3	Unclear
Sanmak 201975	685	30	60	-	2 *	12/4	Unclear
Ulusoy 2017 ⁷⁶	830	50	200	-	3 *	15/3	Yes
Yüzer 200677	904	-	30	-	-	10/1.4	Unclear

*One or more spots/areas treated with movement of the laser probe. LLLT, Low-Level Laser Therapy; WALT, World Association for Laser Therapy.

LLL1, Low-Level Laser Therapy, WAL1, World Association for Laser Therapy.

Overall pain and disability results pain and disability - LLLT versus any control

Data allowing for a meta-analysis of an immediate pain change were available from 16 trials with recommended, non-recommended or unknown laser dosing.

Overall, pain was significantly reduced by LLLT over any control immediately after completed therapy therapy (13.15 mm VAS (95% CI: 7.82 to 18.48), $I^2 = 65\%$, N = 784) (Figure 2) and at follow-ups 4-12 weeks later (12.56 mm VAS (95% CI: 5.69 to 19.42), $I^2 = 48\%$, N = 556) (Figure 3).

Overall, the disability results immediately after completed therapy significantly favoured LLLT over any control (SMD = 0.39 (95% CI: 0.09 to 0.7), $I^2 = 30\%$, N = 260) (Figure 4). A disability reduction by LLLT remained significant at follow-ups 4-9 weeks after completed therapy (SMD = 0.32 (95% CI: 0.05 to 0.59), $I^2 = 4\%$, N = 222) (Figure 5).

Figure 2 Overall pain results immediately after completed therapy - LLLT versus any control AT, Achilles tendinopathy; CT, cryotherapy; ESWT, Extracorporeal Shock Wave Therapy; ET, exercise therapy; I, insoles; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S, stretching; TU, Therapeutic Ultrasound.

Figure 3 Overall pain results at follow-ups - LLLT versus any control

AT, Achilles tendinopathy; CT, cryotherapy; ESWT, Extracorporeal Shock Wave Therapy; ET, exercise therapy; I, insoles; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S, stretching; TU, Therapeutic Ultrasound.

Figure 4 Overall disability results immediately after completed therapy - LLLT versus any control AT, Achilles tendinopathy; CT, cryotherapy; ESWT, Extracorporeal Shock Wave Therapy; ET, exercise therapy; I, insoles; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S = stretching; TU, Therapeutic Ultrasound.

Figure 5 Overall disability results at follow-ups - LLLT versus any control

AT, Achilles tendinopathy; CT, cryotherapy; ET, exercise therapy; I, insoles; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S, stretching.

BMJ Open

Overall and subgroup pain results - LLLT versus placebo-control

Overall, pain was significantly reduced by LLLT over placebo-control immediately after completed therapy (11.48 mm VAS (95% CI: 2.68 to 20.28), $I^2 = 73\%$, N = 507) (Figure 6) and during follow-ups 4-8 weeks after completed therapy (13.62 mm VAS (95% CI: 2.18 to 25.06), $I^2 = 68\%$, N = 277) (Figure 3).

The recommended laser doses significantly reduced pain compared with placebo immediately after completed therapy (14.98 mm VAS (95% CI: 3.74 to 26.22), $I^2 = 67\%$, N = 367) (Figure 6). A non-recommended laser dose from a single trial provided no significant pain reduction immediately after completed therapy (-3.0 mm VAS (95% CI: -11.17 to 5.7), N = 40) (Figure 6). Trials with unknown laser doses significantly favoured LLLT over placebo-control immediately after completed therapy (10.83 mm VAS (95% CI: 2.44 to 19.21), N = 100). The between-subgroup difference was significant (P = 0.02) (Figure 6).

At follow-ups 4-8 weeks after completed therapy, the recommended laser doses significantly reduced pain compared with placebo (14.00 mm VAS (95% CI: 2.81 to 25.19), $I^2 = 5\%$) (supplementary material). A non-recommended dose provided in a single trial did not significantly reduce pain compared with placebo at follow-up 8 weeks after completed therapy (0.00 mm VAS (95% CI: -7.62 to 7.62), N = 40) (supplementary material). At follow-ups 4-5 weeks after completed therapy, trials with unknown laser doses demonstrated a significant pain reduction by LLLT compared with placebo (23.94 mm VAS (95% CI: 14.39 to 33.48), $I^2 = 0\%$, N = 97) (supplementary material). The between-subgroup difference was significant (P = 0.0005) (supplementary material).

Figure 6 Subgroup pain results immediately after completed therapy - LLLT versus placebo-control AT, Achilles tendinopathy; CT, cryotherapy; ET, exercise therapy; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S, stretching.

Subgroup pain results - LLLT versus no intervention

Pain was significantly lowered by the recommended laser doses when used as an adjunct to exercise, stretching and insoles over exercise, stretching and insoles alone, both immediately after completed therapy (18.15 mm VAS (95% CI: 10.55 to 25.76), $I^2 = 0\%$, N = 104) (Figure 7) and at follow-up 9 weeks after completed therapy (19.67 mm VAS (95% CI: 5.16 to 34.18), $I^2 = 0\%$, N = 80) (supplementary material).

Figure 7 Subgroup pain results immediately after completed therapy - LLLT versus no intervention ET, exercise therapy; I, insoles; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S, stretching.

Overall and subgroup pain results - LLLT versus other interventions

Overall, pain was significantly reduced by LLLT compared with other interventions immediately after completed therapy (13.23 mm VAS (95% CI: 4.07 to 22.39), $I^2 = 66\%$, N = 173) (Figure 8). Follow-up results of pain 4-12 weeks after completed therapy favoured LLLT over other interventions, but not significantly (9.41 mm VAS (95% CI: -0.44 to 19.26), $I^2 = 16\%$, N = 193) (supplementary material).

The recommended laser doses were compared with exercise therapy in one trial and ESWT in another trial immediately after completed therapy and the pain results favoured LLLT, but not significantly (13.91 mm VAS (95% CI: -1.34 to 29.15), $I^2 = 65\%$, N = 63) (Figure 8).

The pain results from three trials with unknown laser doses, in which two groups received extracorporeal shock wave therapy (ESWT) and one group received therapeutic ultrasound,

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

favoured LLLT immediately after completed therapy, but not significantly (12.88 mm VAS (95% CI: -1.29 to 27.04), $I^2 = 77\%$, N = 110) (Figure 8).

At follow-ups 4-9 weeks after completed therapy, pain was significantly lowered by the recommended laser doses compared with other interventions (15.90 mm VAS (95% CI: 2.30 to 29.51), $I^2 = 0\%$, N = 103) (supplementary material). Pain was not significantly lowered by unknown laser doses compared with other interventions at follow-ups 4-12 weeks after completed therapy (2.93 mm VAS (95% CI: -15.80 to 21.67), $I^2 = 52\%$, N = 87) (supplementary material).

Figure 8 Overall and subgroup pain results - LLLT versus other interventions

ESWT, Extracorporeal Shock Wave Therapy; ET, exercise therapy; I, insoles; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S = stretching; TU, Therapeutic Ultrasound.

Overall and subgroup disability results - LLLT versus placebo-control

Overall, the disability results favoured LLLT over placebo-control immediately after completed therapy, but not significantly (SMD = 0.2 (95% CI: -0.18 to 0.58), $I^2 = 0\%$, N = 107) (Figure 4). The same applied to the follow-up results 4-8 weeks after completed therapy (SMD = 0.19 (95% CI: -0.11 to 0.49), $I^2 = 0\%$, N = 173) (supplementary material).

The disability results immediately after completed therapy favoured the recommended laser doses over other interventions, but not significantly (SMD = 0.25 (95% CI: -0.21 to 0.7), $I^2 = 0\%$, N = 76) (supplementary material). The same applied to unknown laser doses compared with placebocontrol immediately after completed therapy (SMD = 0.10 (95% CI: -0.61 to 0.80), N = 31) (supplementary material).

At follow-ups 4-8 weeks after completed therapy, the disability results favoured the recommended laser doses over other interventions, but not significantly (SMD = 0.24 (95% CI: - 0.21 to 0.70), I² = 0%, N = 76) (supplementary material). The same applied to the unknown laser doses compared with placebo-control immediately after completed therapy (SMD = 0.14 (95% CI: - 0.26 to 0.54), N = 107) (supplementary material).

Overall and subgroup disability results - LLLT versus other interventions

The overall disability results immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.58 (95% CI: -0.11 to 1.27), $I^2 = 56\%$, N = 90) (figure 4).

The recommended laser doses neither provided a significant disability reduction compared with other interventions immediately after completed therapy (SMD = 0.20 (95% CI: -0.85 to 1.25), N = 14) (supplementary material). The same applied to unknown laser doses compared with other interventions immediately after completed therapy (SMD = 0.73 (95% CI: -0.26 to 1.72), N = 76) (supplementary material).

Subgroup disability results - LLLT versus no intervention

The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), $I^2 = 69\%$, N = 61) (supplementary material). At follow-up 9 weeks after completed therapy, disability was significantly lowered by the recommended laser doses as an adjunct to stretching and insoles compared with exercise therapy and insoles alone (SMD = 0.82 (95% CI: 0.24 to 1.41), N = 49) (supplementary material).

Sensitivity analysis of laser dose categorisation

The irradiation procedure by Darre et al.⁶² was judged as a recommended laser dose, based on the reported dose parameters in the paper. However, the dose description is somewhat sparse and could be misinterpreted. If the study by Darre et al. was allocated to the unknown laser dose subgroup, the

statistical heterogeneity would be eliminated in the recommended laser dose group and the estimated pain reduction would be increased to 21.12 mm VAS ((95% CI: 14.94 to 27.31), $I^2 = 0\%$, N = 278) versus placebo immediately after completed therapy (supplementary material).

Risk-of-bias within studies

Ten of the included trials were found to be of high methodological quality, and the remaining eight included trials were found to be of moderate methodological quality (Table 3). All the trials featured adequate randomisation. Allocation concealment was sufficient in 11 (61%) of the trials. The groups were similar at baseline in 15 (83%) of the trials. The participants were blinded in nine (50%) of the trials. The therapists were blinded in five (28%) of the trials, all of which were placebo-controlled. The assessors were blinded in seven (39%) of the trials, all of which were placebo-controlled. Outcome data were available from more than 15% of the participants in 14 (78%) of the trials. An intention-to-treat analysis was used in 10 (56%) of the trials. A betweengroup statistical comparison was performed in all the trials. Point measures and variability outcome data were stated in 17 (94%) of the trial reports.

The lack of therapist and assessor blinding were the two most obvious methodological inadequacies. However, risk-of-bias subgroup analyses performed post-hoc revealed that there was no significant interaction between the effect estimates and the lack of blinding (supplementary material).

Risk-of-bias across studies (small study/publication bias)

In a random effects model, small and large trials are weighted relatively even when statistical heterogeneity is present. In a fixed effects model, the heterogeneity is ignored and will not influence the weights. Smaller studies in meta-analyses tend to show more positive results than larger trials.⁷⁹ However, there was almost no difference between the pain results of the two meta-analysis models, indicating that no small study bias exists (supplementary material). Likewise, there was no obvious asymmetry in a funnel plot based on the same meta-analyses of pain, indicating that no publication bias was present (supplementary material).

Table 3 PEDro score													
Study ID	Item number												Quality
	1*	2	3	4	5	6	7	8	9	10	11	1	
Basford 199867	+	+	-	+	+	-	+	+	-	+	+	7	High
Cinar 201768	+	+	+	+	-	-	-	+	+	+	+	7	High
Cinar 2018 ⁶⁹	+	+	+	+	-	-	-	+	+	+	+	7	High
Darre 1994 ⁶²	+	+	+	-	+	+	-	-	-	+	-	5	Moderat
													e
Elsehrawy	+	+	-	+	-	-	-	+	-	+	+	5	Moderat
201870													e
Kiritsi 2010 ⁷¹	+	+	+	+	+	+	+	-	-	+	+	8	High
Koteeswaran	+	+	-	+	-	-	-	+	+	+	+	6	Moderat
202072													e
Lamba 2013 ⁷³	+	+	-	+	+	-	-	+	-	+	+	6	Moderat
													e

Liu 2014 ⁶⁰	+	+	-	+	-	-	-	+	+	+	+	6	Moderat
													e
Macias 201574	+	+	+	+	+	-	+	+	+	+	+	9	High
Naterstad ⁶³	+	+	+	+	+	+	+	+	+	+	+	10	High
(unpublished)													
Sanmak 2019 ⁷⁵	+	+	+	+	-	-	-	+	+	+	+	7	High
Stergioulas	+	+	-	+	+	-	+	-	-	+	+	6	Moderat
200361													e
Stergioulas	+	+	+	+	+	-	-	-	+	+	+	8	High
2008 ⁶⁴													
Tumilty 200865	+	+	+	+	+	+	+	+	+	+	+	10	High
Tumilty 2012 ⁶⁶	+	+	+	+	+	+	+	+	+	+	+	10	High
Ulusoy 2017 ⁷⁶	+	+	-	+	-	-	-	+	-	+	+	5	Moderat
													e
Yüzer 200677	+	+	+	+	-	-	-	-	-	+	+	5	Moderat
													e

PEDro, Physiotherapy Evidence Database.

- *Item not included in the mean score.
- 1. Eligibility criteria specified.
- 2. Random allocation.
- 3. Concealed allocation.
- 4. Groups similar at baseline.
- 5. Subject blinding.

- 6. Therapist blinding.
- 7. Assessor blinding.
- 8. Less than 15% dropout.
- 9. Intention-to-treat analysis.
 - 10. Between-group statistical comparisons.
 - 11. Point measures and variability data.

DISCUSSION

We investigated the effectiveness of LLLT in tendon and aponeurosis disorders of the lower extremity. Our overall meta-analysis results demonstrated that pain and disability were statistically significantly reduced by LLLT compared with any control both immediately after completed therapy and in the follow-up period, that is, 4-12 weeks after completed therapy for pain and 4-8 weeks after completed therapy for disability.

review

Like in our previous meta-analysis of LLLT in knee osteoarthritis⁴², we sub-grouped the included trials in the current review using the WALT treatment recommendations.^{58 59} Compared with placebo-control, the recommended laser doses in the current review generally had a larger pain-relieving effect than non-recommended laser both immediately after therapy and in the follow-up period. Similarly, the recommended laser doses had a significant pain-relieving effect as an adjunct to exercise therapy, stretching and insoles both immediately after completed therapy and in the follow-up period. Compared with other treatment modalities, the recommended laser doses were significantly superior, but only at follow-up and only as a pain treatment.

The minimal clinically important improvement (MCII) for pain expressed on the VAS or NRS has not been established for tendinopathy in the lower extremity⁸⁰, even though pain is a prominent feature of this condition. A MCII of 14 mm on a VAS has been suggested in rotator cuff tendinopathy⁸¹, which could indicate that the pain reduction from recommended LLLT doses,

BMJ Open

 compared with placebo-LLLT, is both statistically significant and clinically relevant at the end of treatment (14.98 mm) and at follow-ups (14.0 mm). Prior research indicates that there is a difference in central sensitisation in upper- and lower limb tendinopathy⁸², and thus the transference of MCII from rotator cuff tendinopathy should be considered with some caution. In plantar fasciitis, the MCII for VAS pain has been estimated to be 8 mm for average pain⁸³, and our results are above this threshold in all comparisons.

As for disability, we found that LLLT overall had a small significant effect both immediately after completed therapy and in the follow-up period. Compared with placebo, there were no significant effect of LLLT on disability immediately after completed therapy and at follow-ups. Only Cinar et al.⁶⁸ provided follow-up data on disability regarding LLLT as an add-on to exercise therapy. They found a large and significant positive effect on disability 12 weeks after completed therapy, however, their results are based only on 49 participants⁶⁸, and thus this meta-analysis result should be interpreted with caution.

We were unable to dose categorise the study by Macias et al.⁷⁴ since they used a laser within the visible spectrum (635 nm), which is not mentioned in the WALT treatment guidelines. Light in the red wavelengths (600-700 nm) penetrates the tissue to a lesser extent than light with a wavelength of 700-1000 nm.⁸⁴ Macias et al. utilized a relatively low mean output power, but they stated that they irradiated the tissue for 600 seconds and achieved a significant pain reduction. The methodological quality of their trial⁷⁴ was categorised as high, with a PEDro score of 9.

Sanmak et al.⁷⁵ also used a laser within the red spectrum, but they provided a much smaller dose. Sanmak et al.⁷⁵ compared LLLT with ESWT in plantar fasciitis and found no difference between the groups regarding pain immediately after treatment, but an insignificant better result for ESWT 4 weeks after completed treatment. Comparing LLLT to ESWT, we would expect different time-profiles for pain alleviation, as the effect of ESWT might be better at later time-points.⁸⁵ Sanmak et al.⁷⁵ applied LLLT in a circular motion on the insertion site of the plantar fascia for 60 seconds and along the fascia for another 60 seconds. They stated that they irradiated the tissue with 2 J/cm², which according to our calculation (Watt*seconds) corresponds to a relatively low mean output power of 18 mW/cm². Moving the laser probe during irradiation will yield a smaller laser dose per spot, and larger movement will for instance reduce the energy delivered per cm². Additionally, the skin underneath the heel is thick⁸⁶, and thus absorbs a large percentage of the laser.

We did not identify any trials focusing on trochanter tendinopathy, peroneal or tibialis posterior tendinopathy. In a double-blinded randomised trial by Lögdberg-Andersson et al.⁸⁷, the effect of a 904 nm wavelength laser on participants with trochanteritis was investigated. They found a significant positive effect compared with placebo on pain expressed on a VAS and with algometry, both at the end of treatment and four weeks after.⁸⁷ This trial was not included in our review as we were unable to isolate the participants of interest.

We were only able to identify two randomised controlled trials regarding the effect of LLLT compared with a control in patellar tendinopathy. In a recent clinical trial by Ashok et al.⁸⁸, the effect of LLLT was compared to that therapeutic ultrasound in persons with patellar tendinopathy. They found a statistically significant effect of LLLT compared with therapeutic ultrasound, both in pain reduction and function, however, this trial is small (N = 8) and only of moderate methodological quality. This is consistent with the findings in this review. Another LLLT trial by Meier et al.⁸⁹ included participants with both patellar tendinopathy (N = 58) and Achilles tendinopathy (N = 52), however, we did not include this trial as it solely concerned the effects of an invisible (904 nm wavelength) laser versus a red (632 nm wavelength) laser. They stated that the red laser was placebo but delivered a laser dosage that would be considered possibly effective. Both groups had a positive effect on a combined index of pain and function, favouring the 904 nm laser,

but the trial does not provide point measures or variability data, among other methodological challenges.

The presence and role of inflammation in chronic tendinopathy has been an ongoing debate in the last few decades. There is currently increased support that inflammation has a causal role in tendinopathy, where immune cells and molecular mediators are included as inflammatory components.⁹⁰⁻⁹² Prostaglandin E₂ (PGE₂) has been suggested to sustain inflammation and pain in human tendon disease.⁹³ In Achilles tendinopathy, a reduction of PGE₂ and a concurrent increased pain pressure threshold after LLLT has been found in a double-blinded randomised trial by Bjordal et al.⁹⁴, where microdialysis of the tendon was performed in seven participants. The participants had aggravated the symptoms through a pain inducing activity immediately prior to the examination. Only the immediate (105 minutes) response to LLLT was investigated in the trial, but the findings support the notion that LLLT may act anti-inflammatory in Achilles tendinopathy.

Several authors of the included trials failed to give an adequate description of the laser dose parameters used. A LLLT dose-response relationship has been established in systematic reviews of tendinopathy³⁵⁻³⁷ and osteoarthritis.⁴² In the current review, some of the statistical heterogeneity is plausibly due to the variation in applied laser doses. The statistical heterogeneity of the dose subgroup analyses was generally lower than in the overall (any dose) analyses and this indicates that the dose might be more important for the effect than the location of the tendinopathy. The only study that caused noteworthy statistical heterogeneity in the dose subgroup analysis with placebocontrol was the one by Darre et al.⁶² Most of the pain and disability analyses comparing LLLT with other interventions were performed on plantar fasciitis, and yielded a moderate level of statistical heterogeneity, and it may be explained by the variation in control interventions.

The included trials had a moderate to high methodological quality (mean PEDro score = 7.1). Therapist and assessor blinding lacked in many of the included studies, however, the lack of blinding was not significantly associated with higher effect estimates (supplementary material).

Future trials should be conducted to directly compare the effectiveness of different LLLT parameters. Additionally, systematic reviews of LLLT should include dose-response investigations.

Strengths and limitations of this study

This review was conducted in conformance with a detailed a priori published protocol, which includes, for example, a plan for subgrouping the trials by laser dose. The review includes results from two studies reported in non-English language^{62 77} and an unpublished study.⁶³ The review features meta-analyses with direct comparisons between LLLT and placebo LLLT, other interventions and no intervention. Although only one reviewer extracted data from the included trials, the extracted data was checked for correctness by another reviewer.

CONCLUSIONS

 LLLT reduces pain in lower extremity tendinopathy and plantar fasciitis compared with placebo, other treatments and as an add-on to exercise therapy. LLLT reduces disability to a small extent in the patients. Adhering to the WALT dose recommendations is advised.

Author contributions IFN and MBS wrote the PROSPERO protocol. IFN and MBS selected the trials, with the involvement of JJ when necessary. IFN and MBS judged the risk-of-bias, with the involvement of JJ when necessary. IFN and MBS extracted the data. IFN and MBS translated the non-English articles. IFN performed the analyses, under supervision by MBS. IFN, JJ, JMB, CC, RABLM and MBS participated in interpreting of the results. IFN drafted the first version of the manuscript, and subsequently revised it, based on comments by JJ, JMB, CC, RABLM and MBS. All authors read and accepted the final version of the manuscript.

Acknowledgments None.

Funding The Norwegian Fund for Post-Graduate Training for Physiotherapists funded this research. No other specific grant from any funding agency in the public, commercial or not-for-profit sectors was received for this work. The corresponding author had full access to all data in the study and had the final responsibility for the decision to submit for publication.

- Competing interests JMB and RABLM are former board members and prior presidents of the
 World Association for Laser Therapy, a non-profit research organization from which they have
 never received funding, grants or fees. The other authors declared that they had no conflict of
 interests related to this work.
- Patient and public involvement Patients or the public were not involved in the conceptualisation
 or carrying out of this research.
- **Patient consent for publication** Not required.
- Ethical approval Not required.
 Data availability statement Th

Data availability statement The dataset for meta-analysis is available from the corresponding author upon reasonable request. The corresponding author affirms that the manuscript is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

REFERENCES

- 1. Riel H, Lindstrøm CF, Rathleff MS, et al. Prevalence and incidence rate of lower-extremity tendinopathies in a Danish general practice: a registry-based study. *BMC Musculoskeletal Disorders* 2019;20(1):239. doi: 10.1186/s12891-019-2629-6
- Albers S, Zwerver J, van den Akker-Scheek I. 7 Incidence And Prevalence Of Lower Extremity Tendinopathy In The General Population. *British Journal of Sports Medicine* 2014;48(Suppl 2):A5-A5. doi: 10.1136/bjsports-2014-094114.7
- 3. Janssen I, van der Worp H, Hensing S, et al. Investigating Achilles and patellar tendinopathy prevalence in elite athletics. *Research in Sports Medicine* 2018;26(1):1-12. doi: 10.1080/15438627.2017.1393748
- 4. Wang JH, Iosifidis MI, Fu FH. Biomechanical basis for tendinopathy. *Clinical orthopaedics and related research* 2006;443:320-32. doi: 10.1097/01.blo.0000195927.81845.46 [published Online First: 2006/02/08]
- 5. Magnusson SP, Kjaer M. The impact of loading, unloading, ageing and injury on the human tendon. *J Physiol* 2019;597(5):1283-98. doi: 10.1113/jp275450 [published Online First: 2018/06/20]
- 6. Prichasuk S, Subhadrabandhu T. The relationship of pes planus and calcaneal spur to plantar heel pain. *Clinical orthopaedics and related research* 1994(306):192-6. [published Online First: 1994/09/01]
- Rano JA, Fallat LM, Savoy-Moore RT. Correlation of heel pain with body mass index and other characteristics of heel pain. *J Foot Ankle Surg* 2001;40(6):351-6. doi: 10.1016/s1067-2516(01)80002-8 [published Online First: 2002/01/05]
- Riddle DL, Pulisic M, Pidcoe P, et al. Risk factors for Plantar fasciitis: a matched case-control study. J Bone Joint Surg Am 2003;85(5):872-7. doi: 10.2106/00004623-200305000-00015 [published Online First: 2003/05/03]
- 9. Taunton JE, Ryan MB, Clement DB, et al. A retrospective case-control analysis of 2002 running injuries. *Br J Sports Med* 2002;36(2):95-101. doi: 10.1136/bjsm.36.2.95 [published Online First: 2002/03/28]
- Lemont H, Ammirati KM, Usen N. Plantar fasciitis: a degenerative process (fasciosis) without inflammation. J Am Podiatr Med Assoc 2003;93(3):234-7. doi: 10.7547/87507315-93-3-234
 [published Online First: 2003/05/21]

- 11. Zhang J, Nie D, Rocha JL, et al. Characterization of the structure, cells, and cellular mechanobiological response of human plantar fascia. *J Tissue Eng* 2018;9:2041731418801103. doi: 10.1177/2041731418801103 [published Online First: 2018/10/12]
- 12. van der Vlist AC, Winters M, Weir A, et al. Which treatment is most effective for patients with Achilles tendinopathy? A living systematic review with network meta-analysis of 29 randomised controlled trials. *Br J Sports Med* 2020 doi: 10.1136/bjsports-2019-101872 [published Online First: 2020/06/12]
- 13. Chan KM, Fu SC. Anti-inflammatory management for tendon injuries friends or foes? *Sports Med Arthrosc Rehabil Ther Technol* 2009;1(1):23. doi: 10.1186/1758-2555-1-23 [published Online First: 2009/10/15]
- 14. Aicale R, Bisaccia RD, Oliviero A, et al. Current pharmacological approaches to the treatment of tendinopathy. *Expert Opinion on Pharmacotherapy* 2020;21(12):1467-77. doi: 10.1080/14656566.2020.1763306
- 15. Jomaa G, Kwan C-K, Fu S-C, et al. A systematic review of inflammatory cells and markers in human tendinopathy. *BMC Musculoskeletal Disorders* 2020;21(1):78. doi: 10.1186/s12891-020-3094-y
- 16. Duchman KR, Lemmex DB, Patel SH, et al. The Effect of Non-Steroidal Anti-Inflammatory Drugs on Tendon-to-Bone Healing: A Systematic Review with Subgroup Meta-Analysis. *Iowa Orthop J* 2019;39(1):107-19. [published Online First: 2019/08/16]
- Paoloni JA, Milne C, Orchard J, et al. Non-steroidal anti-inflammatory drugs in sports medicine: guidelines for practical but sensible use. *Br J Sports Med* 2009;43(11):863-5. doi: 10.1136/bjsm.2009.059980 [published Online First: 2009/06/24]
- 18. Bussin ER, Cairns B, Bovard J, et al. Randomised controlled trial evaluating the short-term analgesic effect of topical diclofenac on chronic Achilles tendon pain: a pilot study. *BMJ Open* 2017;7(4):e015126. doi: 10.1136/bmjopen-2016-015126 [published Online First: 2017/05/06]
- 19. Heinemeier KM, Øhlenschlæger TF, Mikkelsen UR, et al. Effects of anti-inflammatory (NSAID) treatment on human tendinopathic tissue. *J Appl Physiol (1985)* 2017;123(5):1397-405. doi: 10.1152/japplphysiol.00281.2017 [published Online First: 2017/09/02]
- 20. Astrom M, Westlin N. No effect of piroxicam on achilles tendinopathy. A randomized study of 70 patients. *Acta orthopaedica Scandinavica* 1992;63(6):631-4. [published Online First: 1992/12/01]
- 21. Bahla NE, J.; Patrono, C.; Baigent, C. et al. . Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials. *The Lancet* 2013;382(9894):769-79. doi: 10.1016/S0140-6736(13)60900-9
- 22. Chung H, Dai T, Sharma SK, et al. The nuts and bolts of low-level laser (light) therapy. Ann Biomed Eng 2012;40(2):516-33. doi: 10.1007/s10439-011-0454-7 [published Online First: 2011/11/03]
- 23. Bjordal JM, Couppe C, Ljunggren AE. Low Level Laser Therapy for Tendinopathy. Evidence of A Dose– Response Pattern. *Physical Therapy Reviews* 2001;6(2):91-99. doi: 10.1179/ptr.2001.6.2.91
 - 24. Mussttaf RA, Jenkins DFL, Jha AN. Assessing the impact of low level laser therapy (LLLT) on biological systems: a review. International Journal of Radiation Biology 2019;95(2):120-43. doi: 10.1080/09553002.2019.1524944
- Bjordal JM, Lopes-Martins RAB, Joensen J, et al. The anti-inflammatory mechanism of low level laser therapy and its relevance for clinical use in physiotherapy. *Physical Therapy Reviews* 2010;15(4):286-93. doi: 10.1179/1743288X10Y.0000000001
- 26. Silveira PC, Silva LA, Fraga DB, et al. Evaluation of mitochondrial respiratory chain activity in muscle healing by low-level laser therapy. *J Photochem Photobiol B* 2009;95(2):89-92. doi: 10.1016/j.jphotobiol.2009.01.004 [published Online First: 2009/02/24]
- Moriyama Y, Moriyama EH, Blackmore K, et al. In vivo study of the inflammatory modulating effects of low-level laser therapy on iNOS expression using bioluminescence imaging. *Photochem Photobiol* 2005;81(6):1351-5. doi: 10.1562/2005-02-28-ra-450 [published Online First: 2005/08/04]

2 3	
4	
5 6	
7	
8	
9 10	
11	
12 13	
14	
15 16	
16 17	
18 19	
20	
21 22	
23	
24 25	
26	
27 28	
29	
30 31	
32	
33 34	
25	
36 37	
38	
39 40	
41	
42 43	
44	
45 46	
47	
48 49	
50	
51 52	
53	
54 55	
56	
57 58	
58 59	
60	

28. Fillipin LI, Mauriz JL, Vedovelli K, et al. Low-level laser therapy (LLLT) prevents oxida reduces fibrosis in rat traumatized Achilles tendon. <i>Lasers Surg Med</i> 2005;37(4	
10.1002/lsm.20225 [published Online First: 2005/10/01] 29. Chen AC, Arany PR, Huang YY, et al. Low-level laser therapy activates NF-kB via gene oxygen species in mouse embryonic fibroblasts. <i>PLoS One</i> 2011;6(7):e22453. do	
10.1371/journal.pone.0022453 [published Online First: 2011/08/05]	
30. Luo L, Sun Z, Zhang L, et al. Effects of low-level laser therapy on ROS homeostasis at 1 and TGF-β1 in skeletal muscle during the repair process. <i>Lasers Med Sci</i> 2013, 10.1007/s10103-012-1133-0 [published Online First: 2012/06/21]	•
31. de Jesus JF, Spadacci-Morena DD, dos Anjos Rabelo ND, et al. Low-level laser therap	oy in IL-1β, COX-2,
and PGE2 modulation in partially injured Achilles tendon. <i>Lasers Med Sci</i> 2015; 10.1007/s10103-014-1636-y [published Online First: 2014/07/30]	
32. Marcos RL, Leal Junior EC, Messias Fde M, et al. Infrared (810 nm) low-level laser th	erany in rat achilles
tendinitis: a consistent alternative to drugs. <i>Photochemistry and photobiology</i> doi: 10.1111/j.1751-1097.2011.00999.x [published Online First: 2011/09/14]	
33. Marcos RL, Leal-Junior EC, Arnold G, et al. Low-level laser therapy in collagenase-ind	duced Achilles
tendinitis in rats: analyses of biochemical and biomechanical aspects. J Orthop	Res
2012;30(12):1945-51. doi: 10.1002/jor.22156 [published Online First: 2012/06/	-
34. Frigo L, Fávero GM, Lima HJC, et al. Low-Level Laser Irradiation (InGaAIP-660 nm) In Cell Proliferation and Reduces Cell Death in a Dose-Dependent Manner. <i>Photor Surgery</i> 2009;28(S1):S-151-S-56. doi: 10.1089/pho.2008.2475	
35. Bjordal JM, Couppe C, Ljunggren AE. Low level laser therapy for tendinopathy. Evide response pattern. <i>Physical Therapy Reviews 2001;6(2):91-99</i> 2001	ence of a dose-
36. Haslerud S, Magnussen LH, Joensen J, et al. The efficacy of low-level laser therapy f	or shoulder
tendinopathy: a systematic review and meta-analysis of randomized controlled <i>Res Int</i> 2015;20(2):108-25. doi: 10.1002/pri.1606 [published Online First: 2014/	trials. Physiother
37. Tumilty S, Munn J, McDonough S, et al. Low level laser treatment of tendinopathy: with meta-analysis. <i>Photomedicine and Laser Surgery 2010 Feb;28(1):3-16</i> 2010	a systematic review
38. Huang YY, Chen AC, Carroll JD, et al. Biphasic dose response in low level light therap	
2009;7(4):358-83. doi: 10.2203/dose-response.09-027.Hamblin [published Onli 2009/12/17]	
39. Huang Y-Y, Sharma SK, Carroll J, et al. Biphasic Dose Response in Low Level Light Th	erapy – an Update.
Dose-Response 2011;9(4):dose-response.11-009.Hamblin. doi: 10.2203/dose-re 009.Hamblin	esponse.11-
40. Zein R, Selting W, Hamblin MR. Review of light parameters and photobiomodulation complexity. <i>Journal of biomedical optics</i> 2018;23(12):1-17. doi:	n efficacy: dive into
http://dx.doi.org/10.1117/1.JBO.23.12.120901	tabiamadulation
41. Hamblin MR. Mechanisms and applications of the anti-inflammatory effects of phote AIMS Biophys 2017;4(3):337-61. doi: 10.3934/biophy.2017.3.337 [published Or 2017/07/28]	
42. Stausholm MB, Naterstad IF, Joensen J, et al. Efficacy of low-level laser therapy on p	pain and disability in
knee osteoarthritis: systematic review and meta-analysis of randomised placeb BMJ Open 2019;9(10):e031142. doi: 10.1136/bmjopen-2019-031142	•
43. Rhim HC, Kim MS, Choi S, et al. Comparative Efficacy and Tolerability of Nonsurgica	Therapies for the
Treatment of Midportion Achilles Tendinopathy: A Systematic Review With Net	

Online First: 2020/07/31] 44. Cabrera Martimbianco AL, Einsfeld Simoes Ferreira RES, de Oliveira Cruz Latorraca C, et al. Photobiomodulation with low-level laser therapy for treating Achilles tendinopathy: a systematic

Orthop J Sports Med 2020;8(7):2325967120930567. doi: 10.1177/2325967120930567 [published

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

ך ע
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
22
23 24
24 25
26 27
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
45 46
40 47
48 49
49 50
50
51
52
53
54
55
56
57
58
59
60

> review and meta-analysis [with consumer summary]. Clinical Rehabilitation 2020 Jun;34(6):713-722 2020 45. Wang W, Jiang W, Tang C, et al. Clinical efficacy of low-level laser therapy in plantar fasciitis: A systematic review and meta-analysis. Medicine (Baltimore) 2019;98(3):e14088. doi: 10.1097/md.0000000000014088 [published Online First: 2019/01/18] 46. Martimbianco ALC, Ferreira RES, Latorraca COC, et al. Photobiomodulation with low-level laser therapy for treating Achilles tendinopathy: a systematic review and meta-analysis. Clinical rehabilitation 2020;34(6):713-22. doi: http://dx.doi.org/10.1177/0269215520912820 47. Dos Santos SA, Sampaio LM, Caires JR, et al. Parameters and Effects of Photobiomodulation in Plantar Fasciitis: A Meta-Analysis and Systematic Review. Photobiomodul Photomed Laser Surg 2019;37(6):327-35. doi: 10.1089/photob.2018.4588 [published Online First: 2019/05/21] 48. Salvioli S, Guidi M, Marcotulli G. The effectiveness of conservative, non-pharmacological treatment, of plantar heel pain: A systematic review with meta-analysis. Foot (Edinb) 2017;33:57-67. doi: 10.1016/j.foot.2017.05.004 [published Online First: 2017/11/11] 49. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and metaanalyses: the PRISMA statement. BMJ 2009;339:b2535. doi: 10.1136/bmj.b2535 50. Wang W, Jiang W, Tang C, et al. Clinical efficacy of low-level laser therapy in plantar fasciitis: A systematic review and meta-analysis. Medicine 2019;98(3):e14088. doi: http://dx.doi.org/10.1097/MD.000000000014088 51. Dos Santos SA, Sampaio LM, Caires JR, et al. Parameters and Effects of Photobiomodulation in Plantar Fasciitis: A Meta-Analysis and Systematic Review. Photobiomodulation, photomedicine, and laser surgery 2019;37(6):327-35. doi: http://dx.doi.org/10.1089/photob.2018.4588 52. de Morton NA. The PEDro scale is a valid measure of the methodological quality of clinical trials: a demographic study. Australian Journal of Physiotherapy 2009;55(2):129-33. doi: https://doi.org/10.1016/S0004-9514(09)70043-1 53. Moseley AM, Herbert RD, Maher CG, et al. Reported quality of randomized controlled trials of physiotherapy interventions has improved over time. Journal of Clinical Epidemiology 2011;64(6):594-601. doi: https://doi.org/10.1016/j.jclinepi.2010.08.009 54. Higgins JP, Green S. Cochrane Handbook for Systematic Reviews of Interventions 2011 [Available from: http://handbook.cochrane.org/. 55. Thong ISK, Jensen MP, Miró J, et al. The validity of pain intensity measures: what do the NRS, VAS, VRS, and FPS-R measure? Scand J Pain 2018;18(1):99-107. doi: 10.1515/sjpain-2018-0012 [published Online First: 2018/05/26] 56. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Statistics in medicine 2002;21(11):1539-58. doi: 10.1002/sim.1186 57. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. Bmj 2003;327(7414):557-60. doi: 10.1136/bmj.327.7414.557 [published Online First: 2003/09/06]

> 58. WALT. Recommended treatment doses for low level laser therapy 780-860 nm wavelength: world association for laser therapy 2010 [Available from: http://waltza.co.za/wp-content/uploads/2012/08/Dose_table_780-860nm_for_Low_Level_Laser_Therapy_WALT-2010.pdf
> 59. WALT. Recommended treatment doses for low level laser therapy 904 nm wavelength: world

59. WALL. Recommended treatment doses for low level laser therapy 904 nm wavelength: world association for laser therapy 2010 [Available from: http://waltza.co.za/wpcontent/uploads/2012/08/Dose_table_904nm_for_Low_Level_Laser_Therapy_WALT-2010.pdf

60. Liu X-G, Cheng L, Song JM. Effects of Low-Level Laser Therapy and Eccentric Exercises in the Treatment of Patellar Tendinopathy. *International Journal of Photoenergy* 2014;2014 doi: 10.1155/2014/785386

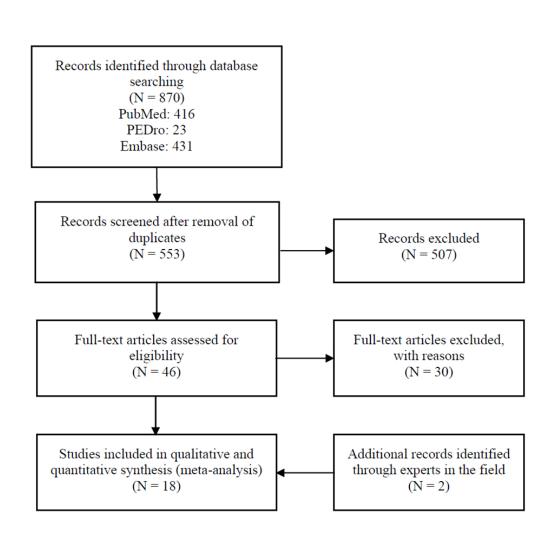
61. Stergioulas A. Effects of a 904 nm GaAs laser versus placebo in the treatment of patellar tendonitis. Laser & Tecnology 2003;13(1-2):21-26.

62. Darre EM, Klokker, M., Lund, P., Rasmussen, J. D., Hansen, K., & Vedtofte, P. E. [Laser Therapy of Achilles Tendinitis]. *Ugeskrift for Laeger* 1994;156(45):6680-83.

<i>с</i> л	Achilles tendinopathy: a double-blinded randomised controlled trial, 2020.
64.	Stergioulas A, Stergioula M, Aarskog R, et al. Effects of low-level laser therapy and eccentric exercise the treatment of recreational athletes with chronic achilles tendinopathy. <i>Am J Sports Med</i> 2008;36(5):881-7. doi: 10.1177/0363546507312165 [published Online First: 2008/02/15]
65	. Tumilty S, Munn J, Abbott JH, et al. Laser therapy in the treatment of Achilles tendinopathy: a pilot study. <i>Photomedicine and Laser Surgery 2008 Feb;26(1):25-30</i> 2008
	Tumilty S, McDonough S, Hurley DA, et al. Clinical effectiveness of low-level laser therapy as an adj to eccentric exercise for the treatment of Achilles' tendinopathy: a randomized controlled tria Archives of Physical Medicine and Rehabilitation 2012 May;93(5):733-739 2012
67.	 Basford JR, Malanga GA, Krause DA, et al. A randomized controlled evaluation of low-intensity lase therapy: plantar fasciitis. Arch Phys Med Rehabil 1998;79(3):249-54. [published Online First: 1998/04/02]
68.	. Cinar E, Saxena S, Uygur F. Low-level laser therapy in the management of plantar fasciitis: a randor controlled trial. <i>Lasers in Medical Science 2018 Jul;33(5):949-958</i> 2018
69.	. Cinar E, Saxena S, Uygur F. Combination therapy versus exercise and orthotic support in the management of pain in plantar fasciitis: a randomized controlled trial. <i>Foot & Ankle Internation 2018 Apr;39(4):406-414</i> 2018
70	Elsehrawy G, Nasef S, Ibrahim M, et al. Extracorporeal Shock Wave Therapy versus Low-Level Laser Therapy in the Management of Chronic Plantar Fasciitis. Suez Canal University Medical Journal 2018;21(2):71-81. doi: 10.21608/scumj.2018.42935
71.	. Kiritsi O, Tsitas K, Malliaropoulos N, et al. Ultrasonographic evaluation of plantar fasciitis after low- laser therapy: results of a double-blind, randomized, placebo-controlled trial. <i>Lasers Med Sci</i> 2010;25(2):275-81. doi: 10.1007/s10103-009-0737-5 [published Online First: 2009/10/21]
72	. Koteeswaran K, Ramya K, Rajeshwari, et al. Effectiveness of low level laser therapy versus ultrasou therapy with plantar fascia streching in subjects with plantar fasciitis. <i>Indian Journal of Public</i> <i>Health Research and Development</i> 2020;11(1):92-96. doi: http://dx.doi.org/10.37506/v11/i1/2020/ijphrd/193792
73.	. Lamba DT, M.; Pankaj, S To Study the Characteristics and efficacy of 820 Nm GA-AI-As Diode Lase the Treatment of Plantar Fasciitis among Porters/Coolies in Kumaun Region, India: A Randomiz Clinical. Indian Journal of Physiotherapy and Occupational Therapy - An International Journal 2013;7(4):34-39.
74.	 Macias DM, Coughlin MJ, Zang K, et al. Low-Level Laser Therapy at 635 nm for Treatment of Chron Plantar Fasciitis: A Placebo-Controlled, Randomized Study. J Foot Ankle Surg 2015;54(5):768-7. doi: 10.1053/j.jfas.2014.12.014 [published Online First: 2015/03/15]
75	 Sanmak ODY, Kulcu DG, Mesci N, et al. Comparison of effects of low-level laser therapy and extracorporeal shock wave therapy in plantar fasciitis treatment: A randomized, prospective, single-blind clinical study. <i>Turkish Journal of Physical Medicine and Rehabilitation</i> 2019;65(2):1 90. doi: http://dx.doi.org/10.5606/tftrd.2019.3528
76.	Ulusoy A, Cerrahoglu L, Orguc S. Magnetic resonance imaging and clinical outcomes of laser therap ultrasound therapy, and extracorporeal shock wave therapy for treatment of plantar fasciitis: randomized controlled trial. <i>The Journal of Foot and Ankle Surgery 2017 Jul-Aug;56(4):762-767</i> 2017
77.	. Yüzer S SS, Gürçay E, Ünlü E, Çakcı A. Comparison of the effectiveness of laser therapy and steroid injection in epin calcanei. <i>Turk J Phys Med Rehabil</i> 2006;52:68-71.
78	Stergioulas A, Stergioula M, Aarskog R, et al. Effects of low-level laser therapy and eccentric exercise the treatment of recreational athletes with chronic Achilles tendinopathy. <i>The American Journ</i> <i>Sports Medicine 2008 May;36(5):881-887</i> 2008

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

- 79. IntHout J, Ioannidis JPA, Borm GF, et al. Small studies are more heterogeneous than large ones: a metameta-analysis. *Journal of Clinical Epidemiology* 2015;68(8):860-69. doi: https://doi.org/10.1016/j.jclinepi.2015.03.017
- 80. Murphy M, Rio E, Debenham J, et al. Evaluating the progress of mid-portion Achilles tendinopathy during rehabilitation: a review of outcome measures for self- reported pain and function. *Int J Sports Phys Ther* 2018;13(2):283-92. [published Online First: 2018/08/10]
- 81. Tashjian RZ, Deloach J, Porucznik CA, et al. Minimal clinically important differences (MCID) and patient acceptable symptomatic state (PASS) for visual analog scales (VAS) measuring pain in patients treated for rotator cuff disease. *Journal of Shoulder and Elbow Surgery* 2009;18(6):927-32. doi: https://doi.org/10.1016/j.jse.2009.03.021
- Plinsinga ML, Brink MS, Vicenzino B, et al. Evidence of Nervous System Sensitization in Commonly Presenting and Persistent Painful Tendinopathies: A Systematic Review. J Orthop Sports Phys Ther 2015;45(11):864-75. doi: 10.2519/jospt.2015.5895 [published Online First: 2015/09/22]
- 83. Landorf KB, Radford JA, Hudson S. Minimal Important Difference (MID) of two commonly used outcome measures for foot problems. *Journal of Foot and Ankle Research* 2010;3(1):7. doi: 10.1186/1757-1146-3-7
- 84. Kwon K, Son T, Lee KJ, et al. Enhancement of light propagation depth in skin: cross-validation of mathematical modeling methods. *Lasers Med Sci* 2009;24(4):605-15. doi: 10.1007/s10103-008-0625-4 [published Online First: 2008/11/26]
- 85. Vulpiani MC, Trischitta D, Trovato P, et al. Extracorporeal shockwave therapy (ESWT) in Achilles tendinopathy. A long-term follow-up observational study. J Sports Med Phys Fitness 2009;49(2):171-6. [published Online First: 2009/06/17]
- 86. Oltulu P, Ince B, Kokbudak N, et al. Measurement of epidermis, dermis, and total skin thicknesses from six different body regions with a new ethical histometric technique. *Turkish Journal of Plastic Surgery* 2018;26(2):56-61. doi: 10.4103/tjps.TJPS_2_17
- 87. Lögdberg-Andersson M MS, Hazel Å. . Low level laser therapy of tendinitis and myofascial pain. A randomised double-blind controlled study. *Laser Therapy* 1997;9:79-86.
- 88. Ashok N, Raghul, S., Sivakumar, V.P.R. Compare The Effects of Low-Level Laser and Ultrasonic Therapy in Subjects with Jumper's Knee. International Journal of Research and Scientific Innovation 2018;V(I)
- 89. Meier JK, K. . Traitement laser de la tendinite. Médecine et hygiène 1988;46(1741):907-11.
 - 90. Millar NL, Dean BJ, Dakin SG. Inflammation and the continuum model: time to acknowledge the molecular era of tendinopathy. *British Journal of Sports Medicine* 2016;50(23):1486.
- 91. Dean BJF, Gettings P, Dakin SG, et al. Are inflammatory cells increased in painful human tendinopathy? A systematic review. *British Journal of Sports Medicine* 2016;50(4):216.
 - 92. Mosca MJ, Rashid MS, Snelling SJ, et al. Trends in the theory that inflammation plays a causal role in tendinopathy: a systematic review and quantitative analysis of published reviews. *BMJ Open Sport Exerc Med* 2018;4(1):e000332. doi: 10.1136/bmjsem-2017-000332 [published Online First: 2018/07/19]
- 93. Bergqvist F, Carr AJ, Wheway K, et al. Divergent roles of prostacyclin and PGE(2) in human tendinopathy. *Arthritis Res Ther* 2019;21(1):74. doi: 10.1186/s13075-019-1855-5 [published Online First: 2019/03/15]
- 94. Bjordal JM, Lopes-Martins RA, Iversen VV. A randomised, placebo controlled trial of low level laser therapy for activated Achilles tendinitis with microdialysis measurement of peritendinous prostaglandin E2 concentrations. *Br J Sports Med* 2006;40(1):76-80; discussion 76-80. doi: 10.1136/bjsm.2005.020842 [published Online First: 2005/12/24]



195x184mm (120 x 120 DPI)

BMJ Open: first published as 10.1136/bmjopen-2021-059479 on 28 September 2022. Downloaded from http://bmjopen.bmj.com/ on June 10, 2025 at Agence Bibliographique de I Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

BMJ Open

Enseignement Superieur (ABES). Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.	Open: first published as 10.1136/bmjopen-2021-059479 on 28 September 2022. Downloaded from http://bmjopen.bmj.com/ on June 10, 2025 at Agence Bibliogram
--	--

lue de l

Study or Subgroup		LLLT		C C	ontrol			Mean Difference	Mean Difference
	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.1.1 LLLT vs placebo									
Darre 1994, LLLT vs placebo LLLT in AT	40.5	37.91	46	52	34.37	43	5.4%	-11.50 [-26.52, 3.52]	
Tumilty 2012, LLLT+ET vs placebo LLLT+ET in AT	6	17.1	20	9	7.45	20	7.8%	-3.00 [-11.17, 5.17]	-+
Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT	22.6	29.9	10	17.2	17.75	10	3.7%	5.40 [-16.15, 26.95]	<u> </u>
Basford 1998, LLLT vs placebo LLLT in PF	34.4	45.58	16	26.1	29.26	15	2.8%	8.30 [-18.50, 35.10]	
Macias 2015, LLLT vs placebo LLLT in PF	19.8	22.49	37	8.7	14.56	32	7.6%	11.10 [2.27, 19.93]	
Naterstad, LLLT+ET+CT vs placebo LLLT+ET+CT in AT	28.9	29.18	20	11.54	35.09	21	4.1%	17.36 [-2.36, 37.08]	
Kiritsi 2010, LLLT vs placebo LLLT in PF	40	20.3	25	18	8.9	25	7.6%	22.00 [13.31, 30.69]	
Lamba 2013, LLLT+S vs placebo LLLT+S in PF	32	53	40	8.3	53	40	3.4%	23.70 [0.47, 46.93]	
Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT	24.8	25	26	0	25	26	5.9%	24.80 [11.21, 38.39]	
Stergioulas 2003, LLLT vs placebo LLLT in PT	35.5	71.04	18	6.4	12.39	17	2.0%	29.10 [-4.24, 62.44]	
Subtotal (95% CI)			258			249	50.4%	11.48 [2.68, 20.28]	-
Heterogeneity: Tau ² = 126.14; Chi ² = 32.84, df = 9 (P = 0 Test for overall effect: Z = 2.56 (P = 0.01)	.0001); I²	= 73%							
1.1.2 LLLT vs no intervention									
Liu 2014, LLLT+ET vs ET in PT	62.86	10.4	7	46.43	10.69	7	6.8%	16.43 [5.38, 27.48]	
Cinar 2018, LLLT+S+I vs S+I in PF	38	24.9	24	20	25.28	17	5.3%	18.00 [2.39, 33.61]	
Cinar 2017, LLLT+S+I vs S+I in PF Subtotal (95% CI)	38.8	28.6	27 58	17.7	21.92	22 46	5.7% 17.7%	21.10 [6.95, 35.25] 18.15 [10.55, 25.76]	•
Heterogeneity: Tau ² = 0.00; Chi ² = 0.26, df = 2 (P = 0.88) Test for overall effect: Z = 4.68 (P < 0.00001)	; I ² = 0%								
1.1.3 LLLT vs other intervention									
Sanmak 2019, LLLT vs ESWT in PF	10	20.16	17	10	19.23	17	6.0%	0.00 [-13.24, 13.24]	
Liu 2014, LLLT vs ET in PT	52.86	12.2	7	46.43	10.69	7	6.4%	6.43 [-5.59, 18.45]	+
Elsehrawy 2018, LLLT+S vs ESWT+S in PF	57	15.45	23	46	15.45	23	7.5%	11.00 [2.07, 19.93]	
Cinar 2018, LLLT+S+I vs ESWT+S+I in PF	38	24.9	24	16	23.1	25	5.9%	22.00 [8.54, 35.46]	
Koteeswaran 2020, LLLT+S vs TU+S in PF Subtotal (95% CI)	35.4	25.6	15 86	7.4	6.01	15 87	6.0% 31.9%	28.00 [14.69, 41.31] 13.23 [4.07, 22.39]	•
Heterogeneity: Tau ² = 70.74; Chi ² = 11.63, df = 4 (P = 0.0 Test for overall effect: Z = 2.83 (P = 0.005)	02); l ² = 6	5%							
Total (95% CI)			402			382	100.0%	13.15 [7.82, 18.48]	•

336x207mm (120 x 120 DPI)

		LLLT		(Control			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% (
2.1.1 LLLT vs placebo									
Tumilty 2012, LLLT+ET vs placebo LLLT+ET in AT	15	11.75	20	15	12.82	20	14.7%	0.00 [-7.62, 7.62]	-
Naterstad, LLLT+ET+CT vs placebo LLLT+ET+CT in AT	26.59	36.46	20	22.99	29.18	21	7.0%	3.60 [-16.68, 23.88]	
Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT	30.9	31.73	10	20	20	10	5.9%	10.90 [-12.35, 34.15]	
Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT	17.9	26.6	20	0	26.6	20	8.8%	17.90 [1.41, 34.39]	
Basford 1998, LLLT vs placebo LLLT in PF	37.4	62.57	15	19.4	61.92	13	2.0%	18.00 [-28.21, 64.21]	
Macias 2015, LLLT vs placebo LLLT in PF	29.6	24.9	37	5.4	16	32	13.2%	24.20 [14.45, 33.95]	
Stergioulas 2003, LLLT vs placebo LLLT in PT Subtotal (95% CI)	60.6	88.57	18 140	17.3	21.87	17 133	2.3% 53.9%	43.30 [1.08, 85.52] 13.62 [2.18, 25.06]	•
Heterogeneity: Tau ² = 130.26; Chi ² = 18.51, df = 6 (P = 0. Test for overall effect: Z = 2.33 (P = 0.02)	.005); l² =	68%							
2.1.2 LLLT vs other intervention									
Sanmak 2019, LLLT vs ESWT in PF	20	32.64	17	30	39.76	17	5.5%	-10.00 [-34.45, 14.45]	
Ulusoy 2017, LLLT+ET+S vs ESWT+ET+S in PF	39.4	40.41	8	38.6	44.4	20	3.3%	0.80 [-33.30, 34.90]	
Ulusoy 2017, LLLT+ET+S vs TU+ET+S in PF	39.4	40.41	9	31	31.8	17	4.0%	8.40 [-22.02, 38.82]	
Yuzer 2006, LLLT vs steroid injection in PF	48	22.91	26	38	23.32	30	11.5%	10.00 [-2.13, 22.13]	
Cinar 2018, LLLT+S+I vs ESWT+S+I in PF Subtotal (95% CI)	44	24.9	24 84	22	35.13	25 109	8.6% 32.8%	22.00 [5.00, 39.00] 9.41 [-0.44, 19.26]	•
Heterogeneity: Tau ² = 21.59; Chi ² = 4.77, df = 4 (P = 0.31 Test for overall effect: Z = 1.87 (P = 0.06)); I ² = 169	6							
2.1.3 LLLT vs no intervention									
Cinar 2018, LLLT+S+I vs S+I in PF	44	26.05	24	27	29.17	17	8.4%	17.00 [-0.35, 34.35]	
Cinar 2017, LLLT+S+I vs S+I in PF	44.1	61.76	27	18.2	30.15	22	4.9%	25.90 [-0.58, 52.38]	
Subtotal (95% CI)			51			39	13.3%	19.67 [5.16, 34.18]	
Heterogeneity: Tau ² = 0.00; Chi ² = 0.30, df = 1 (P = 0.58); Test for overall effect: $Z = 2.66$ (P = 0.008)	l² = 0%								
Total (95% CI)			275			281	100.0%	12.56 [5.69, 19.42]	•
Heterogeneity: Tau ² = 68.06; Chi ² = 25.08, df = 13 (P = 0.	0.00.17	000	210			201		12100 [0100, 10142]	· · · · · · ·

336x182mm (120 x 120 DPI)

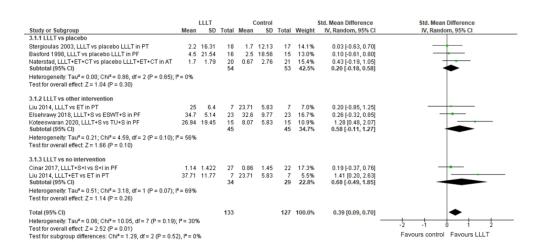
For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open

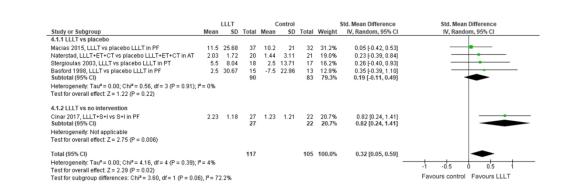
1	
1	
2	
3	
5	
4	
5	
6	
7	
8	
0	
9	
10	
11	
12	
13	
14	
15	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	
40	
41	
42	
43	
44	
45	
46	
47	
48	
49	
50	
51	
52	
53	
54	
55	

57 58 59

60



338x153mm (120 x 120 DPI)



338x111mm (120 x 120 DPI)

BMJ Open

Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.	AJ Open: first published as 10.1136/bmjopen-2021-059479 on 28 September 2022. Downloaded from http://bmjopen.bmj.com/ on June 10, 2025 at Agence Bibliographi
---	---

Non-statement	Study or subgroup Mean SD Total SD SD <	Study or Subgroup Mean SD Total Weight V, Random, 95% CI V, Random, 95% CI Dare 1994, LLT-vs placebo LLT-in total 45 37.91 46 52 34.31 10.95 11.56 56.21 35.01 10.95 10.15 10.95 10.15 56.21 35.01 10.95 10.15 10.95 10.15 26.25 56.01 16.15 26.37.08 10.95 10.15 10.95 10.15 26.25 50.11 10.95 10.15 10.95 10.95 10.95 20.11 30.95 10.95	Study or subgroupMeanSDTotalWeightV, Random, 95% CIV, Random, 95% CIDare 1994, LLT ve placebo LLT ve fin Ares bull: T+ET not Kash45.537.11465234.3710.9811.5610.95% CIV, Random, 95% CIDare 1994, LLT ve placebo LLT ve fin Ares bull: T+ET not Kash42.653.911017.117.110.9811.5612.88.2%54.01 E81 (5.2.66.3)Harbs 2013, LLT ve placebo LLT +ET not T26.929.182011.5435.09218.9%17.36 (2.2.6.26)Harbs 2013, LLT ve placebo LLT +ET not T28.925188.227.10 (4.14, 6.8.3)Stergioulas 2003, LLT ve splacebo LLT +ET in AT24.8252602529.11 (4.8, 6.2.4)Stergioulas 2003, LLT ve splacebo LLT +ET in AT24.825202529.11 (4.24, 6.2.4)Heterogeneity: Tar# 14.0.53, Ch* = 18.27, df = 6 (P = 0.006); P = 67%12.97.452014.0%-3.00 [+11.17, 5.17]Subtola (95% CI11.14 Fe Ve placebo LLT +ET in AT617.12097.452014.0%-3.00 [+11.17, 5.17]Subtola (95% CI11.14 Fe Ve placebo LLT +ET in AT617.12097.452014.0%-3.00 [+11.17, 5.17]Subtola (95% CI11.14 Fe Ve placebo LLT +ET in AT617.12097.452014.0%-3.00 [+11.17, 5.17]Subtola (95% CI11.48 Fe Ve placebo11.14 Fe Ve placebo11.14 Fe Ve placebo11.10 Fe Ve placebo <th></th> <th></th> <th>BMJ Open</th> <th></th> <th></th> <th>P</th>			BMJ Open			P
Study or subgroup Mean SD Total SD SD SD SD SD SD SD SD SD <th>Study or subgroup Mean SD Total SD SD <</th> <th>Study or Subgroup Mean SD Total Weight V, Random, 95% CI V, Random, 95% CI Dare 1994, LLT-vs placebo LLT-in total 45 37.91 46 52 34.31 10.95 11.56 56.21 35.01 10.95 10.15 10.95 10.15 56.21 35.01 10.95 10.15 10.95 10.15 26.25 56.01 16.15 26.37.08 10.95 10.15 10.95 10.15 26.25 50.11 10.95 10.15 10.95 10.95 10.95 20.11 30.95 10.95</th> <th>Study or subgroupMeanSDTotalWeightV, Random, 95% CIV, Random, 95% CIDare 1994, LLT ve placebo LLT ve fin Ares bull: T+ET not Kash45.537.11465234.3710.9811.5610.95% CIV, Random, 95% CIDare 1994, LLT ve placebo LLT ve fin Ares bull: T+ET not Kash42.653.911017.117.110.9811.5612.88.2%54.01 E81 (5.2.66.3)Harbs 2013, LLT ve placebo LLT +ET not T26.929.182011.5435.09218.9%17.36 (2.2.6.26)Harbs 2013, LLT ve placebo LLT +ET not T28.925188.227.10 (4.14, 6.8.3)Stergioulas 2003, LLT ve splacebo LLT +ET in AT24.8252602529.11 (4.8, 6.2.4)Stergioulas 2003, LLT ve splacebo LLT +ET in AT24.825202529.11 (4.24, 6.2.4)Heterogeneity: Tar# 14.0.53, Ch* = 18.27, df = 6 (P = 0.006); P = 67%12.97.452014.0%-3.00 [+11.17, 5.17]Subtola (95% CI11.14 Fe Ve placebo LLT +ET in AT617.12097.452014.0%-3.00 [+11.17, 5.17]Subtola (95% CI11.14 Fe Ve placebo LLT +ET in AT617.12097.452014.0%-3.00 [+11.17, 5.17]Subtola (95% CI11.14 Fe Ve placebo LLT +ET in AT617.12097.452014.0%-3.00 [+11.17, 5.17]Subtola (95% CI11.48 Fe Ve placebo11.14 Fe Ve placebo11.14 Fe Ve placebo11.10 Fe Ve placebo<th></th><th></th><th></th><th></th><th></th><th></th></th>	Study or subgroup Mean SD Total SD SD <	Study or Subgroup Mean SD Total Weight V, Random, 95% CI V, Random, 95% CI Dare 1994, LLT-vs placebo LLT-in total 45 37.91 46 52 34.31 10.95 11.56 56.21 35.01 10.95 10.15 10.95 10.15 56.21 35.01 10.95 10.15 10.95 10.15 26.25 56.01 16.15 26.37.08 10.95 10.15 10.95 10.15 26.25 50.11 10.95 10.15 10.95 10.95 10.95 20.11 30.95 10.95	Study or subgroupMeanSDTotalWeightV, Random, 95% CIV, Random, 95% CIDare 1994, LLT ve placebo LLT ve fin Ares bull: T+ET not Kash45.537.11465234.3710.9811.5610.95% CIV, Random, 95% CIDare 1994, LLT ve placebo LLT ve fin Ares bull: T+ET not Kash42.653.911017.117.110.9811.5612.88.2%54.01 E81 (5.2.66.3)Harbs 2013, LLT ve placebo LLT +ET not T26.929.182011.5435.09218.9%17.36 (2.2.6.26)Harbs 2013, LLT ve placebo LLT +ET not T28.925188.227.10 (4.14, 6.8.3)Stergioulas 2003, LLT ve splacebo LLT +ET in AT24.8252602529.11 (4.8, 6.2.4)Stergioulas 2003, LLT ve splacebo LLT +ET in AT24.825202529.11 (4.24, 6.2.4)Heterogeneity: Tar# 14.0.53, Ch* = 18.27, df = 6 (P = 0.006); P = 67%12.97.452014.0%-3.00 [+11.17, 5.17]Subtola (95% CI11.14 Fe Ve placebo LLT +ET in AT617.12097.452014.0%-3.00 [+11.17, 5.17]Subtola (95% CI11.14 Fe Ve placebo LLT +ET in AT617.12097.452014.0%-3.00 [+11.17, 5.17]Subtola (95% CI11.14 Fe Ve placebo LLT +ET in AT617.12097.452014.0%-3.00 [+11.17, 5.17]Subtola (95% CI11.48 Fe Ve placebo11.14 Fe Ve placebo11.14 Fe Ve placebo11.10 Fe Ve placebo <th></th> <th></th> <th></th> <th></th> <th></th> <th></th>						
Dare 1994, LLT vs placebo LLT in AT 40.5 37.91 46 52 34.37 43 10.98 -11.50 [26.52, 35.2] Turnily 2008, LLT vs placebo LLT v FT vn AT 22.6 29 10 17.2 17.75 10 8.2% 5.40 [15.6, 26.8] Naterstad, LLT vs placebo LLT v FT vn AT 22.6 29 10 20.3 25 18 8.9 25 13.8% 22.07 [0.4.7, 46.33] Stergiouls 2003, LLT vs placebo LLT v FT in AT 24.8 25 26 0 25 26 11.6% 24.80 [11.21, 38.39] Stergiouls 2003, LLT vs placebo LLT v FT in AT 24.8 25 26 0 2.5 26 11.6% 24.80 [12.1, 28.39] Stergiouls 2003, LLT vs placebo LLT v FT in AT 6 (7.1 20 9 7.45 20 14.0% -3.00 [-11.17, 5.17] Subtotal (95% C) 5.1.2 Non-recommended LLT dose vs placebo Turnily 2012, LLT +ET vs placebo LLT v FT in AT 6 17.1 20 9 7.45 20 14.0% -3.00 [-11.17, 5.17] Subtotal (95% C) 5.1.2 Non-recommended LLT dose vs placebo Turnily 2012, LLT vs Placebo LLT v FT in AT 6 17.1 20 9 7.45 20 14.0% -3.00 [-11.17, 5.17] Subtotal (95% C) 5.1.2 Non-recommended LLT dose vs placebo Turnily 2012, LLT vs Placebo LLT v FT in AT 6 17.1 20 9 7.45 20 14.0% -3.00 [-11.17, 5.17] Subtotal (95% C) 5.1.2 Non-recommended LLT dose vs placebo Turnily 2012, LLT vs Placebo LLT vs PT 13.8 22.49 37 8.7 14.56 32 13.8% 11.10 [2.27, 19.39] 5.3 47 20.2% 10.83 [2.44, 19.21] Heterogeneity, Tau" = 128, 14, Ch" = 32.84, df = 9 (P = 0.000); P = 78.1% Test for overall effect Z = 2.53 (P = 0.01) Test for overall effect Z = 2.54 (P = 0.02), P = 76.1% Test for overall effect Z = 2.54 (P = 0.02), P = 76.1% Test for overall effect Z = 2.54 (H = 0.02), P = 76.1%	Dare 1994, LLT vs placebo LLT in AT 40.5 37.91 46 52 34.37 43 10.98 -11.50 [2.652, 3.52] Turnihj 2008, LLT +ET vs placebo LLT +ET + OT in AT 26.9 20.18 2.99 10 17.2 17.75 10 8.2% 5.40 [1.51, 26.86] Naterstad, LLT +ET vs placebo LLT +ET + OT in AT 26.9 20.18 2.9 21 18 8.9 21 8.89 2.70 [0.47, 46.33] Stergiouls 2008, LLT +ET vs placebo LLT +ET in AT 24.8 2.5 26 0. 2.5 26 11.6% 24.80 [1.21, 38.39] Stergiouls 2003, LLT +ET vs placebo LLT +ET in AT 24.8 2.5 26 0. 2.5 26 11.6% 24.80 [1.21, 28.39] Stergiouls 2003, LLT +ET vs placebo LLT +ET in AT 24.8 2.5 26 0. 2.5 26 11.6% 24.80 [1.21, 28.39] Stergiouls 2003, LLT +ET vs placebo LLT +ET in AT 6 17.1 20 9 7.45 20 14.0% -3.00 [-11.17, 5.17] Subtoal (9% C) 5.1.2 Non-recommended LLT dose vs placebo Turnih; 2012, LLT +ET vs placebo LLT +ET in AT 6 17.1 20 9 7.45 20 14.0% -3.00 [-11.17, 5.17] Subtoal (9% C) 5.1.2 Non-recommended LLT hose vs placebo Turnih; 2012, LLT +ET vs placebo LLT +ET in AT 6 17.1 20 9 7.45 20 14.0% -3.00 [-11.17, 5.17] Subtoal (9% C) 5.1.2 Non-recommended LLT hose vs placebo Turnih; 2012, LLT +ET vs placebo LLT +ET in AT 6 17.1 20 9 7.45 20 14.0% -3.00 [-11.17, 5.17] Subtoal (9% C) 5.1.2 Non-recommended LLT hose vs placebo Turnih; 2012, LLT +ET vs placebo LLT +ET in AT 6 17.1 20 9 7.45 22 14.0% -3.00 [-11.17, 5.17] Subtoal (9% C) 5.1.2 Non-recommended LLT hose vs placebo Turnih; 2012, LLT +S placebo LLT +ET in AT 6 17.1 20 9 7.45 22 14.0% -3.00 [-11.17, 5.17] Subtoal (9% C) 5.1.2 Non-recommended LLT hose vs placebo Turnih; 2012, LLT +S placebo LLT +ET in AT 52.6 22.1 29.26 15 6.4% 8.30 [-18.50, 35.10] Macias 2015, LLT vs placebo LLT +ET in AT 52.6 22.1 29.26 15 6.4% 8.30 [-18.50, 35.10] Turnih; 2012, LLT +S placebo LLT +ET in AT 52.6 22.1 29.26 15 6.4% 8.30 [-18.50, 35.10] Turnih; 2012, LLT +S placebo LLT +ET in AT 52.6 22.28 1.50 - 50 - 50 - 50 - 50 - 50 - 50 - 50 -	Dare 1994, LLT vs placebo LLT in AT 40.5 37.91 46 52 34.97 43 10.98 1.150 [26.52, 35.2] Turmity 2008, LLT vs placebo LLT vs Tin AT 26.8 29.10 17.2 17.75 10 8.2% 5.40 [1.51, 26.89] Nateriad, LLT vs placebo LLT vs Fir AT 22.8 29.18 20 11.54 35.09 21 8.98 23.01 1.33, 13.08 [Lamba 2013, LLT vs placebo LLT in PF 40 20.3 25 18 8.9 25 13.8% 22.01 0.47, 46.83 [Stergiouis 2000, LLT vs placebo LLT in FF 32.5 71.04 18 6.4 12.39 1152 65.7% 14.96 [3.74, 24.82.4] Heterogeneity, Tau" = 140.53, Ch" = 18.27, df = 6 (P = 0.006), P = 67% [Test for overall effect Z = 2.81 (P = 0.009) [P = 77% [Test for overall effect Z = 0.72 (P = 0.47) 5.1 19.8 22.49 37 8.7 14.56 22 15 6.4% 8.30 [18.50, 35.10] [Heterogeneity, Tau" = 140, Ch" = 32.84, df = 9 (P = 0.000); P = 76.1% [Test for overall effect Z = 2.53 (P = 0.01) [P = 0.000]; P = 76.1% [Test for overall effect Z = 2.53 (P = 0.001); P = 76.1% [Test for overall effect Z = 2.54 (f = 0.000); P = 76.1% [Test for overall effect Z = 2.56 (P = 0.000); P = 76.1% [Test for overall effect Z = 2.56 (P = 0.001); P = 78.1% [Test for overall effect Z = 2.56 (P = 0.002), P = 76.1% [Test for overall effect Z = 2.56 (P = 0.001); P = 76.1% [Test for overall effect Z = 2.56 (P = 0.002), P = 76.1% [Test for overall effect Z = 2.56 (P = 0.002), P = 76.1% [Test for overall effect Z = 2.56 (P = 0.002), P = 76.1% [Test for overall effect Z = 2.56 (P = 0.002), P = 76.1% [Test for overall effect Z = 2.56 (P = 0.002), P = 76.1% [Test for overall effect Z = 2.56 (P = 0.002), P = 76.1% [Test for overall effect Z = 2.56 (P = 0.002), P = 76.1% [Test for overall effect Z = 2.56 (P = 0.002), P = 76.1% [Test for overall effect Z = 2.56 (P = 0.002), P = 76.1% [Test for overall effect Z = 2.56 (P = 0.002), P = 76.1% [Test for overall effect Z = 2.56 (P = 0.002), P = 76.1% [Test for overall effect Z = 2.56 (P = 0.002), P = 76.1% [Test for overall effect Z = 2.56 (P = 0.002), P = 76.1% [Test for overall effect Z = 2.56 (P = 0.002), P = 76.1% [Test for overall effect	Dare 1994, LLT vs placebo LLT Fin AT 40.5 37.91 46 52 34.37 43 10.9% 11.150 ; 26.52, 35.21 (min) 2008, LLT Fit Vs placebo LLT Fit AT 226 29.10 17.27 17.5 10 8.2% 5.40 [Fit 5, 26.8] (min) 2019, LLT vs placebo LLT Fit FIT AT 28.9 2019 2019, 25.2 35.21 8.9% 17.38 (F.2.36, 27.08) 21.89% 12.00 (MLT vs placebo LLT Vs placebo LLT VS PI A 2000, 25.5 10.8 (MLT VS PLACE NOL LLT VS PI A 2000, LLT VS PLACE NOL LLT VS PI A 2000, LLT VS PLACE NOL LLT VS PI A 2000, LLT VS PLACE NOL LLT VS PI A 2000, LLT VS PLACE NOL LLT VS PI A 2000, LLT VS PLACE NOL PS VS PLACE NOL VS PLAC						
Turnity 2012, LLT+ET vs placebo LLLT+ET in AT 6 17.1 20 9 7.45 20 14.0% -3.00 [+11.17, 5.17] Subtotal (95% C) 20 14.0% -3.00 [+11.17, 5.17]	Turnity 2012, LLT+ET vs placebo LLLT+ET in AT 6 17.1 20 9 7.45 20 14.0% -3.00 [+11.17, 5.17] Subtotal (95% CI) 20 14.0% -3.00 [+11.17, 5.17]	Turnity 2012, LLT+ET vs placebo LLLT+ET in AT 6 17.1 20 9 7.45 20 14.0% -3.00 [+11.17, 5.17] Heterogeneity. Not applicable 20 14.0% -3.00 [-11.17, 5.17] 20 Fest for overall effect Z = 0.72 (P = 0.47) 5.1.3 Unknown LLLT dose vs placebo 5.1.3 Unknown LLLT dose vs placebo LLLT in PF 9.8 24.9 37 8.7 14.56 32 13.8% 11.10 [2.27, 19.93] Stubtotal (95% CI) 18.8 20.4 4.4 4.56.8 32 13.8% 11.10 [2.27, 19.93] Stubtotal (95% CI) 53 47 20.2% 10.83 [2.44, 19.21] 4.4 Heterogeneity: Tau* = 0.00; Ch* = 0.04, df = 1 (P = 0.85); P = 0% 53 47 20.2% 10.83 [2.44, 19.21] Test for overall effect Z = 2.53 (P = 0.01) 258 249 100.0% 11.48 [2.68, 20.28] Heterogeneity: Tau* = 126.14; Ch* = 32.84, df = 9 (P = 0.0001); P = 73% 258 249 100.0% 11.48 [2.68, 20.28] Test for overall effect Z = 2.56 (P = 0.01) Favours placebo Favours placebo Favours placebo Favours placebo Test for subgroup differences: Ch* = 8.38, df = 2 (P = 0.02), P = 76.1% Favours placebo	Turnity 2012, LLT-FET ws placebo LLLT-FET in AT 6 17.1 20 9 7.45 20 14.0% -3.00 [+11.17, 51.7] Subtotal (95% Cf) 20 14.0% -3.00 [+11.7, 51.7] 20 14.0% -3.00 [+11.7, 51.7] Subtotal (95% Cf) 51.3 Unknown LLLT dose vs placebo 16 26.1 29.26 15 6.4% 8.30 [+18.50, 35.10] Macias 2015, LLLT vs placebo LLLT in PF 19.8 22.49 37 8.7 14.56 32 13.8% 11.10 [2.27, 19.93] Subtotal (95% Cf) 19.8 22.49 53 47 20.2% 10.83 [2.44, 19.21] Heterogeneity: Tau* = 10.01; Chi* = 0.04; df = 1 (P = 0.85); P = 0% 53 47 20.2% 10.83 [2.44, 19.21] Total (95% Cf) 258 249 100.0% 11.48 [2.68, 20.28] -100 -50 50 100 Festfor verail effect Z = 2.56 (P = 0.01) 258 249 100.0% 11.48 [2.68, 20.28] -100 -50 50 100 Festfor verail effect Z = 2.66 (P = 0.01) 73% 78.7 14.56 258 249 100.0% 11.48 [2.68, 20.28] -100 -50 <td>Darre 1994, LLLT vs placebo LLLT in AT Turnilly 2008, LLLT+ET vs placebo LLLT+ET in AT Naterstad, LLT+ET-CT vs placebo LLLT+ET+CT in AT Kirtisi 2010, LLLT vs placebo LLLT in PF Lamba 2013, LLLT+S vs placebo LLLT+S in PF Stergioulas 2003, LLLT+Vs placebo LLLT+S in AT Stergioulas 2003, LLLT vs placebo LLLT in PT Subtotal (95% CI) Heterogeneity, Tau² = 140.53; Ch² = 18.27, df = 6 (P = 0.01)</td> <td>22.6 29.9 11 28.9 29.18 21 40 20.3 22 32 53 41 24.8 25 21 35.5 71.04 11 18</td> <td>10 17.2 17.75 10 20 11.54 35.09 21 25 18 8.9 25 40 8.3 53 40 26 0 25 26 18 6.4 12.39 17</td> <td>8.2% 5.40 [-16.15, 26.95] 8.9% 17.36 [-2.36, 37.08] 13.8% 22.00 [13.31, 30.69] 7.6% 23.70 [0.47, 46.93] 11.6% 24.80 [11.21, 38.39] 4.9% 29.10 [-4.24, 62.44]</td> <td>+</td> <td>-</td>	Darre 1994, LLLT vs placebo LLLT in AT Turnilly 2008, LLLT+ET vs placebo LLLT+ET in AT Naterstad, LLT+ET-CT vs placebo LLLT+ET+CT in AT Kirtisi 2010, LLLT vs placebo LLLT in PF Lamba 2013, LLLT+S vs placebo LLLT+S in PF Stergioulas 2003, LLLT+Vs placebo LLLT+S in AT Stergioulas 2003, LLLT vs placebo LLLT in PT Subtotal (95% CI) Heterogeneity, Tau ² = 140.53; Ch ² = 18.27, df = 6 (P = 0.01)	22.6 29.9 11 28.9 29.18 21 40 20.3 22 32 53 41 24.8 25 21 35.5 71.04 11 18	10 17.2 17.75 10 20 11.54 35.09 21 25 18 8.9 25 40 8.3 53 40 26 0 25 26 18 6.4 12.39 17	8.2% 5.40 [-16.15, 26.95] 8.9% 17.36 [-2.36, 37.08] 13.8% 22.00 [13.31, 30.69] 7.6% 23.70 [0.47, 46.93] 11.6% 24.80 [11.21, 38.39] 4.9% 29.10 [-4.24, 62.44]	+	-
Basford 1998, LLLT vs placebo LLLT in PF 34.4 45.8 16 26.1 29.26 15 6.4% 8.30 [18.50, 35.10] Macias 2015, LLLT vs placebo LLLT in PF 19.8 22.49 37 8.7 14.56 32 13.8% 11.10 [2.27, 19.93] Subtotal (95% Cl) Total (95% Cl)	Basford 1998, LLLT vs placebo LLLT in PF 34.4 45.58 16 26.1 29.26 15 6.4% 8.30 [18.50, 35.10] Macias 2015, LLLT vs placebo LLLT in PF 19.8 22.49 37 8.7 14.56 32 13.8% 11.10 [2.27, 19.93] Subtotal (95% Cl) Total (95% Cl)	Basford 1998, LLLT vs placebo LLLT in PF 34.4 45.58 16 26.1 29.26 15 6.4% 8.30 [18.50, 35.10] Macias 2015, LLT vs placebo LLLT in PF 18.8 22.49 37 8.7 14.56 32 13.8% 11.10 [2.27, 19.93] Subtotal (95% Cl) Total (95% Cl)	Basford 1998, LLLT vs placebo LLLT in PF 34.4 45.58 16 26.1 29.26 15 6.4% 8.30 [16.50, 35.10] Macias 2015, LLT vs placebo LLLT in PF 19.8 22.49 37 8.7 14.56 32 13.8% 11.10 [2.27, 19.93] Subtotal (95% Cl) Total (95% Cl)	Turnilty 2012, LLLT+ET vs placebo LLLT+ET in AT Subtotal (95% CI) Heterogeneity: Not applicable	6 17.1 2/ 2/	20 9 7.45 20 20 20 20	14.0% -3.00 [-11.17, 5.17] 14.0% -3.00 [-11.17, 5.17]	•	
Total (95% Cl) 258 249 100.0% 11.48 [2.68, 20.28] Heterogeneity: Tau" = 126.14; Chi" = 32.84, df = 9 (P = 0.0001); P = 73% 100 -50 50 100 Test for overall effect Z = 2.56 (P = 0.01) -50 0 50 100 Test for subgroup differences: Chi" = 8.38, df = 2 (P = 0.02), P = 76.1% Favours placebo Favours LLLT	Total (95% Cl) 258 249 100.0% 11.48 [2.68, 20.28] Heterogeneity: Tau" = 126.14; Chi" = 32.84, df = 9 (P = 0.0001); P = 73% 100 -50 50 100 Test for overall effect Z = 2.56 (P = 0.01) -50 0 50 100 Test for subgroup differences: Chi" = 8.38, df = 2 (P = 0.02), P = 76.1% Favours placebo Favours LLLT	Total (95% Cl) 258 249 100.0% 11.48 [2.68, 20.28] Heterogeneity: Tau ² = 126.14; Chi ² = 32.84, df = 9 (P = 0.0001); P = 73% -100 -50 0 50 100 Test for subgroup differences: Chi ² = 8.38, df = 2 (P = 0.02), P = 76.1% Favours placebo Favours LLLT	Total (95% CI) 258 249 100.0% 11.48 [2.68, 20.28] Heterogeneity. Tau ² = 126.14; Chi ² = 32.84, df = 9 (P = 0.0001); I ² = 73% Test for overall effect Z = 2.56 (P = 0.01) Test for subgroup differences: Chi ² = 8.38, df = 2 (P = 0.02), I ² = 76.1% Test for subgroup differences: Chi ² = 8.38, df = 2 (P = 0.02), I ² = 76.1%	Basford 1998, LLLT vs placebo LLLT in PF Macias 2015, LLLT vs placebo LLLT in PF Subtotal (95% CI) Heterogeneity: Tau ² = 0.00; Chi ² = 0.04, df = 1 (P = 0.85); P	19.8 22.49 3 5	37 8.7 14.56 32	13.8% 11.10 [2.27, 19.93]		
				Total (95% CI) Heterogeneity: Tau ² = 126.14; Chi ² = 32.84, df = 9 (P = 0.01 Test for overall effect: Z = 2.56 (P = 0.01)	001); I² = 73%	58 249 1	00.0% 11.48 [2.68, 20.28]	-100 -50 0 50 100	

1	
2	
3	
4 5	
6	LLLT Control Mean Difference Mean Difference
7	Study or Subgroup Mean SD Total Weight IV, Random, 95% CI IV, Random, 95% CI Liu 2014, LLLT+ET vs ET in PT 62.86 10.4 7 46.43 10.69 7 47.4% 16.43 [5.38, 27.48]
8	Lu 2014, LLL 1+S+1 vs S+1 in PF 38 24.9 24 20 25.28 17 23.7% 18.00 [2.39, 23,61]
9	Total (95% CI) 58 46 100.0% 18.15 [10.55, 25.76]
10	Heterogeneity: Tau ² = 0.00; Chi ² = 0.26, df = 2 (P = 0.88); I ² = 0% Test for overall effect: Z = 4.68 (P < 0.00001) Favours control Favours LLLT
11 12	
13	
14	324x55mm (120 x 120 DPI)
15	524x55mm (120 x 120 D11)
16	
17 18	
18	
20	
21	
22	
23	
24 25	
26	
27	
28	
29	
30 31	
32	
33	
34	
35	
36	
37 38	
39	
40	
41	
42	
43 44	
45	
46	
47	
48	
49 50	
51	
52	
53	
54	
55 56	
57	
58	
59	
60	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open

LLLT Mean Differenc Mean Difference Contro
 Study or Subgroup
 Mean

 9.3.1 Recommended LLLT dose vs other intervention
 Liu 2014, LLLT vs ET in PT
 52.86
 1
 SD Total Mean SD Total Weight IV, Random, 95% CI IV, Random, 95% Cl 12.2 46.43 10.69 20.2% 6.43 [-5.59, 18.45] Cinar 2018, LLLT+S+I vs ESWT+S+I in PF Subtotal (95% CI) 24.9 31 23.1 32 18.5% 38.7% 22.00 [8.54, 35.46] 13.91 [-1.34, 29.15] Heterogeneity: Tau² = 78.83; Chi² = 2.86, df = 1 (P = 0.09); I² = 65% Test for overall effect: Z = 1.79 (P = 0.07) 9.3.2 Unknown LLLT dose vs other intervention 10 19.23 46 15.45 7.4 6.01 23 15 55 18.8% 23.9% 18.7% 61.3% Sanmak 2019, LLLT vs ESWT in PF Elsehrawy 2018, LLLT+S vs ESWT+S in PF 10 20.16 57 15.45 23 15 55 0.00 [-13.24, 13.24] 11.00 [2.07, 19.93] Koteeswaran 2020, LLLT+S vs TU+S in PF Subtotal (95% CI) 35.4 25.6 28.00 [14.69, 41.31] 12.88 [-1.29, 27.04] Heterogeneity: Tau² = 120.11; Chi² = 8.74, df = 2 (P = 0.01); l² = 77% Test for overall effect: Z = 1.78 (P = 0.07) Total (95% CI) 87 100.0% 13.23 [4.07, 22.39] $\label{eq:constraint} \begin{array}{l} \mbox{Heterogeneity: Tau^2 = 70.74; Chi^2 = 11.63, df = 4 (P = 0.02); l^2 = 66\% \\ \mbox{Test for overall effect: Z = 2.83 (P = 0.005) \\ \mbox{Test for subgroup differences: Chi^2 = 0.01, df = 1 (P = 0.92), l^2 = 0\% \\ \end{array}$ -50 -25 Favours control

326x117mm (120 x 120 DPI)

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

39 BMJ Open: first published as 10.1136/bmjopen-2021-059479 on 28 September 2022. Downloaded from http://bmjopen.bmj.com/ on June 10, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies. Page

Supplemental digital content for the article:

Efficacy of low-level laser therapy in patients with lower extremity tendinopathy or plantar fasciitis: systematic review and meta-analysis of randomised controlled trials

Contents								
PubMed database search string2								
Table of excluded full text articles								
Pain at follow-ups 4-8 weeks after completed therapy - LLLT versus placebo								
Pain at follow-ups 4-12 weeks after completed therapy - LLLT versus other interventions								
Disability immediately after completed therapy - LLLT versus placebo								
Disability at follow-ups 4-8 weeks after completed therapy - LLLT versus placebo								
Disability immediately after completed therapy - LLLT versus other interventions								
Disability immediately after completed therapy - LLLT versus no intervention								
Disability at follow-up 9 weeks after completed therapy - LLLT versus no intervention								
Sensitivity analyses								
Risk-of-bias within studies post-hoc analyses6								
Risk-of-bias across studies - random versus fixed effects meta-analysis results of pain								
Risk-of-bias between studies - funnel plot8								

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

1 2 3 4 5 6 7 8 9 10 11 12 13	PubMed database search string ("Low-Level Light Therapy"[Mesh] OR LLLT[Title/Abstract] OR "low level"[Title/Abstract] OR "low power"[Title/Abstract] OR laser therap*[Title/Abstract] OR "laser acupuncture"[Title/Abstract] OR "HeNe"[Title/Abstract] OR "632 nm"[Title/Abstract] OR "Ga-Al-As"[Title/Abstract] OR "820 nm"[Title/Abstract] OR "830 nm"[Title/Abstract] OR "850 nm"[Title/Abstract] OR "GaAs"[Title/Abstract] OR "904 nm"[Title/Abstract] OR Photobiomodulation[Title/Abstract] OR phototherap*[Title/Abstract]) and ("Tendinopathy"[Mesh] or tendi*[Title/Abstract] or tendo*[Title/Abstract] or "plantar fasciitis"[Title/Abstract] or "Fasciitis, Plantar"[Mesh] or "Policeman's Heel"[Title/Abstract] or "Iliotibial Band Syndrome"[Mesh] or Iliopsoas tendi*[Title/Abstract] or Jumper*[Title/Abstract] or Patella[Title/Abstract] or Achill*[Title/Abstract] or "Achilles Tendon"[Mesh]) Table of excluded full text articles										
14	Table of excluded full text an	rticles									
15	Author/Year/Reference	Reasons for exclusion									
16	Abat et al. 2016 ¹	Impossible to isolate effect, combined treatments compared with other treatment									
17	Aigner et al. 1996 ²	No control group									
18	Ashok et al. 2018 ³	Lacks randomisation									
19	Atik et al. 2018 ⁴										
20	Bjordal et al. 2006 ⁵	Outcomes of interest not reported Outcomes of interest not reported									
21	Chang et al. 2015 ⁶										
22	Cinar et al. 2013 ⁷	Conference paper only (author contacted)									
23	Cinar et al. 2012 ⁸	Solely abstract available									
24	Costantino et al. 2005 ⁹	Not LLLT, high intensity laser therapy									
25	Coughlin et al. 2014 ¹⁰	Solely abstract available									
26	Fernandes et al. 1991 ¹¹	Mixed population with unclear inclusion of diagnosis									
27	Foley et al. 2016 ¹²	Not LLLT, light emitting diode therapy									
28	Jastifer et al. 2014 ¹³	No control group									
29	Lögdberg-Andersson et al. 1994 ¹⁴	Only pooled data on lower and upper extremity available									
30	Mardh et al. 2016 ¹⁵	Not LLLT, high intensity laser therapy									
31	Meier et al. 1988 ¹⁶	Outcomes of interest not reported									
32	Morimoto et al. 2013 ¹⁷	No control group									
33	Mulcahy et al. 1995 ¹⁸	Lacks credible control group, includes only 3 patients with tendinopathy									
34	Notarnicola et al. 2014 ¹⁹	Not LLLT, high intensity laser therapy									
35	Olivera et al. 2009 ²⁰	Animal study									
36	Orellana-Molina et al. 2010 ²¹	Outcomes of interest not reported									
37	Saxena et al. 2015 ²²	Not LLLT									
38	Scott et al. 2011 ²³	Review									
39	Siebert et al. 1987 ²⁴	Mixed population/diagnoses									
40	Simunovic 1996 ²⁵	Narrative review									
41	Suleymanoglu et al. 2014 ²⁶	Conference abstract									
42	Takla et al. 2019 ²⁷	Used a combination of LLLT and light emitting diode therapy									
43	Tumilty et al. 2015 ²⁸	Conference abstract									
44	Tumilty et al. 2016 ²⁹	Not LLLT, high intensity laser therapy									
45 46	LLLT, low-level laser therapy.										

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

33

34

35 36 37

BMJ Open

Pain at follow-ups 4-8 weeks after completed therapy - LLLT versus placebo

1			LLLT	1	C	Control		- <u> </u> - <u></u>	Mean Difference	Mean Difference
2	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
	6.1.1 Recommended LLLT vs placebo									
3	Naterstad, LLLT+ET+CT vs placebo LLLT+ET+CT in AT		36.46			29.18	21	14.4%	3.60 [-16.68, 23.88]	
4	Turnilty 2008, LLLT+ET vs placebo LLLT+ET in AT Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT	30.9	31.73 26.6	10 20	20 0	20 26.6	10 20		10.90 [-12.35, 34.15] 17.90 [1.41, 34.39]	
5	Stergioulas 2003, LLLT vs placebo LLLT in PT Subtotal (95% CI)		88.57	18 68		21.87	17 68	5.7% 49.6%	43.30 [1.08, 85.52] 14.00 [2.81, 25.19]	→
6	Heterogeneity: Tau ² = 6.48; Chi ² = 3.14, df = 3 (P = 0.37); F Test for overall effect: Z = 2.45 (P = 0.01)	²= 5%								
7 8 9 10	6.1.2 Non-recommended LLLT vs placebo Turnilly 2012, LLLT+ET vs placebo LLLT+ET in AT Subtotal (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.00 (P = 1.00)	15	11.75	20 20	15	12.82	20 20	23.4% 23.4%	0.00 [-7.62, 7.62] 0.00 [-7.62, 7.62]	•
11 12 13 14	6.1.3 Unknown LLLT dose vs placebo Basford 1998, LLLT vs placebo LLLT in PF Macias 2015, LLLT vs placebo LLLT in PF Subtotal (95% CI) Heterogeneity: Tau ² = 0.00; Chi ² = 0.07, df = 1 (P = 0.80); F Test for overall effect: Z = 4.92 (P < 0.00001)	29.6	62.57 24.9	15 37 52	19.4 5.4	61.92 16	13 32 45	22.0%	18.00 [-28.21, 64.21] 24.20 [14.45, 33.95] 23.94 [14.39, 33.48]	 ◆
15 16 17	Total (95% CI) Heterogeneity: Tau ² = 130.26; Chi ² = 18.51, df = 6 (P = 0.0 Test for overall effect: Z = 2.33 (P = 0.02) Test for subgroup differences: Chi ² = 15.28, df = 2 (P = 0.0			140			133	100.0%	13.62 [2.18, 25.06]	-50 -25 0 25 50 Favours placebo Favours LLLT
18	Figure S1: Pain at follow-ups 4-	8 we	eks	afte	r cor	nnle	hted	thera	ny - IIIT vei	rsus placebo

Figure S1: Pain at follow-ups 4-8 weeks after completed therapy - LLLT versus placebo
 AT, Achilles tendinopathy; CT, cryotherapy; ESWT, Extracorporeal Shock Wave Therapy; ET, exercise
 therapy; I, insoles; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S,
 stretching; TU, Therapeutic Ultrasound.

Pain at follow-ups 8 weeks after completed therapy - LLLT versus no intervention

26	1		LLLT		0	Control		1	Mean Difference		Mean D	fference	
27	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rando	om, 95% Cl	
28	Cinar 2018, LLLT+S+I vs S+I in PF	44	26.05	24	27	29.17	17	70.0%	17.00 [-0.35, 34.35]				
29	Cinar 2017, LLLT+S+I vs S+I in PF	44.1	61.76	27	18.2	30.15	22	30.0%	25.90 [-0.58, 52.38]				
30	Total (95% CI)			51			39	100.0%	19.67 [5.16, 34.18]				
31	Heterogeneity: Tau ² = 0.00; Chi ² = 0.3	30, df = 1	l (P = 0.	58); l² =	= 0%					-50	-25	1 1 0 25	50
32	Test for overall effect: Z = 2.66 (P = 0	.008)								-30	Favours control		50

Figure S2: Pain at follow-ups 8 weeks after completed therapy - LLLT versus no intervention ET, exercise therapy; I, insoles; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; S, stretching.

38				
39	Pain at follow-ups 4-12 weeks after	completed therapy	/ - LLLT versus other	interventions
		Control	Mean Difference	Mean Difference

40			LLLT		C	ontrol			Mean Difference	Mean Difference
40	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	I IV, Random, 95% CI
41	10.3.1 Recommended LLLT dose vs other interve	ention								
42	Ulusoy 2017, LLLT+ET+S vs ESWT+ET+S in PF	39.4	40.41	8	38.6	44.4	20	7.8%	0.80 [-33.30, 34.90]]
	Ulusoy 2017, LLLT+ET+S vs TU+ET+S in PF	39.4	40.41	9	31	31.8	17	9.6%	8.40 [-22.02, 38.82]]
43	Cinar 2018, LLLT+S+I vs ESWT+S+I in PF	44	24.9	24	22	35.13	25	26.1%	22.00 [5.00, 39.00]	
44	Subtotal (95% CI)			41			62	43.5%	15.90 [2.30, 29.51]	
45	Heterogeneity: Tau ² = 0.00; Chi ² = 1.48, df = 2 (P =	0.48); l²	= 0%							
	Test for overall effect: Z = 2.29 (P = 0.02)									
46										
47	10.3.3 Unknown LLLT dose vs other intervention									
	Sanmak 2019, LLLT vs ESWT in PF	20	32.64	17	30	39.76	17	14.3%	-10.00 [-34.45, 14.45]]
48	Yuzer 2006, LLLT vs steroid injection in PF	48	22.91	26	38	23.32	30	42.2%	10.00 [-2.13, 22.13]	
49	Subtotal (95% CI)			43			47	56.5%	2.93 [-15.80, 21.67]	
	Heterogeneity: Tau ² = 103.01; Chi ² = 2.06, df = 1 (F	P = 0.15)	; I ² = 52	%						
50	Test for overall effect: Z = 0.31 (P = 0.76)									
51										
52	Total (95% CI)			84			109	100.0%	9.41 [-0.44, 19.26]	
	Heterogeneity: Tau ² = 21.59; Chi ² = 4.77, df = 4 (P =	= 0.31);	l² = 169	5						-50 -25 0 25 50
53	Test for overall effect: Z = 1.87 (P = 0.06)									Favours control Favours LLLT
	Test for subgroup differences: ChiZ = 4.04 df = 4.//	n – o hz	12 - 45	2.00/						ratedio control Tarouro EEET

54 Test for subgroup differences: $Chi^2 = 1.21$, df = 1 (P = 0.27), $l^2 = 17.0\%$

Figure S3: Pain at follow-ups 4-12 weeks after completed therapy - LLLT versus other interventions
 AT, Achilles tendinopathy; CT, cryotherapy; ESWT, Extracorporeal Shock Wave Therapy; ET, exercise
 therapy; I, insoles; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S,
 stretching; TU, Therapeutic Ultrasound.

Disability immediately after completed therapy - LLLT versus placebo

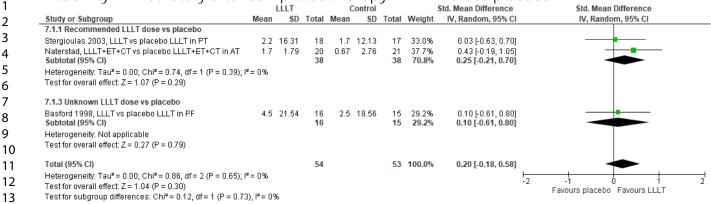


Figure S4: Disability immediately after completed therapy - LLLT versus placebo 14

15 AT, Achilles tendinopathy; CT, cryotherapy; ET, exercise therapy; LLLT, Low-Level Laser Therapy; PF, 16 plantar fasciitis; PT, patellar tendinopathy. 17

19 Disability at follow-ups 4-8 weeks after completed therapy - LLLT versus placebo 20

20							0.0			
1			LLLT		C	ontrol		:	Std. Mean Difference	Std. Mean Difference
1	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
2	8.1.1 Recommended LLLT dose vs placebo									
3	Naterstad, LLLT+ET+CT vs placebo LLLT+ET+CT in AT	2.03	1.72	20	1.44	3.11	21	23.8%	0.23 [-0.39, 0.84]	
)	Stergioulas 2003, LLLT vs placebo LLLT in PT	5.5	8.04	18	2.5	13.71	17	20.2%	0.26 [-0.40, 0.93]	
L	Subtotal (95% CI)			38			38	44.0%	0.24 [-0.21, 0.70]	
;	Heterogeneity: Tau ² = 0.00; Chi ² = 0.01, df = 1 (P = 0.94); l ² =	= 0%								
)	Test for overall effect: Z = 1.06 (P = 0.29)									
5	0.4.2 University I.I.T. does up placebo									
,	8.1.3 Unknown LLLT dose vs placebo									
	Macias 2015, LLLT vs placebo LLLT in PF		25.68	37	10.2	21	32	40.1%	0.05 [-0.42, 0.53]	_
3	Basford 1998, LLLT vs placebo LLLT in PF	2.5	30.67	15	-7.5	22.96	13	16.0%	0.35 [-0.39, 1.10]	
	Subtotal (95% CI)			52			45	56.0%	0.14 [-0.26, 0.54]	
	Heterogeneity: Tau ² = 0.00; Chi ² = 0.44, df = 1 (P = 0.51); l ² =	= 0%								
)	Test for overall effect: Z = 0.69 (P = 0.49)									
	Total (95% CI)			90			03	100.0%	0.19 [-0.11, 0.49]	
		~~		90			00	100.0%	0.19[-0.11, 0.49]	
2	Heterogeneity: Tau ² = 0.00; Chi ² = 0.56, df = 3 (P = 0.91); l ² =	= 0%								-1 -0.5 0 0.5 1
	Test for overall effect: Z = 1.22 (P = 0.22)		~							Favours placebo Favours LLLT
3	Test for subgroup differences: Chi ² = 0.11, df = 1 (P = 0.73),	$1^{*} = 0.9$	%							

34 Figure S5: Disability at follow-ups 4-8 weeks after completed therapy - LLLT versus placebo 35 AT, Achilles tendinopathy; CT, cryotherapy; ET, exercise therapy; LLLT, Low-Level Laser Therapy; PF, 36 plantar fasciitis; PT, patellar tendinopathy. 37

39 Disability immediately after completed therapy - LLLT versus other interventions 40

	·····						- T - J	/		
1			LLLT		C	ontrol			Std. Mean Difference	Std. Mean Difference
	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
2	11.3.1 Recommended LLLT dose vs other in	iterventi	on							
3	Liu 2014, LLLT vs ET in PT	25	6.4	7	23.71	5.83	7	25.0%	0.20 [-0.85, 1.25]	
ł	Subtotal (95% CI)			7			7	25.0%	0.20 [-0.85, 1.25]	
	Heterogeneity: Not applicable									
5	Test for overall effect: Z = 0.37 (P = 0.71)									
б	11.3.2 Unknown LLLT dose vs other interve	ntion								
7	Elsehrawy 2018, LLLT+S vs ESWT+S in PF	34.7	5.14	23	32.6	9.77	23	41.8%	0.26 [-0.32, 0.85]	
3	Koteeswaran 2020, LLLT+S vs TU+S in PF	26.94	19.45	15	8.07	5.83	15	33.2%	1.28 [0.48, 2.07]	_
	Subtotal (95% CI)			38			38	75.0%	0.73 [-0.26, 1.72]	
)	Heterogeneity: Tau ² = 0.39; Chi ² = 4.07, df = 1	(P = 0.0	4); ² = 1	75%						
)	Test for overall effect: Z = 1.45 (P = 0.15)									
	Total (95% CI)			45			45	100.0%	0.58 [-0.11, 1.27]	
)	Heterogeneity: Tau ² = 0.21; Chi ² = 4.59, df = 2	(P = 0.1	0); I ^z = :	56%						
-	Test for overall effect: Z = 1.66 (P = 0.10)									Favours control Favours LLLT
3	Test for subgroup differences: Chi ² = 0.53, df	= 1 (P =	0.47), P	²= 0%						avours control 1 avours EEET
1										

Figure S6: Disability immediately after completed therapy - LLLT versus other interventions 55 56 ET, exercise therapy; ESWT, Extracorporeal Shock Wave Therapy; LLLT, Low-Level Laser Therapy; PF, 57 plantar fasciitis; PT, patellar tendinopathy; S, stretching; TU, Therapeutic Ultrasound. 58

1

7

18

Page 33 of 39

BMJ Open

Study or Subgroup Mean SD	Total	Mean	SD T	otal We			Difference dom, 95% Cl	IV, R	Random, 95% Cl
Cinar 2017, LLLT+S+I vs S+I in PF 1.14 1.422 Liu 2014, LLLT+ET vs ET in PT 37.71 11.77		0.86 23.71			.2% .8%		[-0.37, 0.76] [0.20, 2.63]		
Total (95% CI)	34			29 100	.0%	0.68	[-0.49, 1.85]		
Heterogeneity: Tau ² = 0.51; Chi ² = 3.18, df = 1 (P = 0 Test for overall effect: Z = 1.14 (P = 0.26)		69%		20 100		0100		-2 -1 avours no interve	0 1 2 ntion Favours LLLT
Figure S7: Disability immediately	y afte	r con	nplete	ed the	rapy	- LL	LT versus r	no interven	tion
ET, exercise therapy; I, insoles; L	LLT	, Lov	v-Lev	vel La	ser 7	Therap	py; PF, plar	ntar fasciiti	s; PT, patellar
tendinopathy; S, stretching.									
Disability at follow-up 9 week	ks aft			leted					
LLLT Study or Subgroup Mean SD T	Total M	Conti ean S		l Weigh		Mean Dif , Randon	terence n, 95% Cl		in Difference dom, 95% Cl
Cinar 2017, LLLT+S+I vs S+I in PF 2.23 1.18	27 1	1.23 1.2	21 23	2 100.09	6	0.82 [0.	.24, 1.41]		
Total (95% CI)	27		22	2 100.09	6	0.82 [0.	24, 1.41]		
Heterogeneity: Not applicable Test for overall effect: Z = 2.75 (P = 0.006)								-1 -0.5	0 0.5 1
	0	a a 1 a a	often		1.4.4.4.4	1 41		urs no intervention	
Figure S8: Disability at follow-up									
ET, exercise therapy; I, insoles; L	LLT	, Lov	v-Lev	vel La	ser	heraj	py; PF, plar	itar fasciiti	is; PT, patellar
tendinopathy; S, stretching.									
Sensitivity analyses									
Allocating the study by Darre et a									
Allocating the study by Darre et a heterogeneity in the recommended	d lase	er do	se sul	bgrou	p an	d incr	eases the es	stimate of j	placebo-controlle
Allocating the study by Darre et a heterogeneity in the recommender reduction to 21.12 mm VAS ((95)	d lase	er do	se sul	bgrou	p an	d incr	eases the es	stimate of j	placebo-controlle
Allocating the study by Darre et a heterogeneity in the recommended	d lase % CI	er dos : 14.9	se sul	bgrou	p an	d incr	eases the es	stimate of j	placebo-controlle ly after complete
Allocating the study by Darre et a heterogeneity in the recommender reduction to 21.12 mm VAS ((959 therapy (Figure S9).	d lase % CI ۱	er dos : 14.9	se sul 94 to	bgrouj 27.31 Control	p an), I ²	d incr = 0%	reases the est, $N = 278$	stimate of j immediate	placebo-controlle ly after complete Mean Difference
Allocating the study by Darre et a heterogeneity in the recommender reduction to 21.12 mm VAS ((959 therapy (Figure S9).	d lase % CI Mean	er dos : 14.9	se sul 94 to ^{Total Me}	27.31 Control	p and), I ²	d incr = 0% Weight	reases the es , $N = 278$) Mean Difference IV, Random, 95%	stimate of j immediate	placebo-controlle ly after complete
Allocating the study by Darre et a heterogeneity in the recommender reduction to 21.12 mm VAS ((959 therapy (Figure S9). <u>Study or Subgroup</u>	d lase % CI <u>Mean</u> 40.5	er dos : 14.9	se sul 94 to ^{Total Me} 46	bgrouj 27.31 Control	p and), I ² Total	d incr = 0%	reases the est, $N = 278$	stimate of j immediate	placebo-controlle ly after complete Mean Difference
Allocating the study by Darre et a heterogeneity in the recommender reduction to 21.12 mm VAS ((95% therapy (Figure S9). <u>Study or Subgroup</u> 5.1.1 Recommended LLLT dose vs placebo Darre 1994, LLLT vs placebo LLLT in AT Turnily 2008, LLLT+ET vs placebo LLLT+ET in AT Naterstad, LLLT+ET+CT vs placebo LLLT+ET+CT in AT	d lase % CI <u>Mean</u> 40.5 22.6 28.9	er dos : 14.9 	se sul 94 to ^{fotal Me} 46 10 17 20 11.	bgrouj 27.31 control an SD 52 34.37 7.2 17.75 54 35.09	p and), I ² Total 43 10 21	d incr = 0% <u>Weight</u> 0.0% 8.2% 8.9%	reases the est, $N = 278$) Mean Difference IV, Random, 95% -11.50 [-26.52, 3.5; 5.40 [-16.15, 26.9] 17.36 [-2.36, 37.0]	ci ^{2]}	placebo-controlle ly after complete Mean Difference
Allocating the study by Darre et a heterogeneity in the recommender reduction to 21.12 mm VAS ((959 therapy (Figure S9). <u>Study or Subgroup</u> 5.1.1 Recommended LLLT dose vs placebo Darre 1994, LLLT vs placebo LLLT in AT Tumilty 2008, LLLT+ET vs placebo LLLT in AT Naterstad, LLLT+ET+CT vs placebo LLLT+ET in AT Kirtsi 2010, LLLT vs placebo LLLT in PF	d lase % CI <u>Mean</u> 40.5 22.6 28.9 40	er dos : 14.9 :	se sul 94 to 6 10 17 20 11. 25	bgrouj 27.31 Control an SD 52 34.37 7.2 17.75 .54 35.09 18 8.9	p and), I ² Total 43 10 21 25	d incr = 0% <u>Weight</u> 0.0% 8.2% 8.9% 13.8%	reases the est, $N = 278$) Mean Difference IV, Random, 95% -11.50 [-26.52, 3.5 5.40 [-16.15, 26.9 17.36 [-2.36, 37.0) 22.00 [13.31, 30.6]	ci 2] 5] 6] 6] 6] 6] 6] 6] 6] 6] 6] 6	placebo-controlle ly after complete Mean Difference
Allocating the study by Darre et a heterogeneity in the recommender reduction to 21.12 mm VAS ((95° therapy (Figure S9). <u>Study or Subgroup</u> <u>5.1.1 Recommended LLLT dose vs placebo</u> Darre 1994, LLLT vs placebo LLLT in AT Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT Naterstad, LLLT+ET+CT vs placebo LLLT+ET in AT Kiritsi 2010, LLLT vs placebo LLLT in PF Lamba 2013, LLLT+S vs placebo LLLT in PF Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT	d lase % CI <u>Mean</u> 40.5 22.6 28.9 40 32 24.8	er dos : 14.9 : 14.9 : 14.9 : 14.9 : 14.9 : 29.9 : 29.9 : 29.9 : 29.9 : 29.9 : 29.9 : 29.9 : 29.9 : 29.3 : 53 : 25	se sul 94 to 6 10 17 20 11. 25	bgrouj 27.31 control an SD 52 34.37 7.2 17.75 54 35.09	p and), I ² Total 43 10 21 25 40	d incr = 0% <u>Weight</u> 0.0% 8.2% 8.9%	reases the est, $N = 278$) Mean Difference IV, Random, 95% -11.50 [-26.52, 3.5; 5.40 [-16.15, 26.9] 17.36 [-2.36, 37.0]	ci 2] 2] 2] 2] 2] 2] 2] 2] 2] 2]	placebo-controlle ly after complete Mean Difference
Allocating the study by Darre et a heterogeneity in the recommender reduction to 21.12 mm VAS ((95% therapy (Figure S9). <u>Study or Subgroup</u> <u>5.1.1 Recommended LLLT dose vs placebo</u> Dare 1994, LLLT vs placebo LLLT in AT Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT Naterstad, LLLT+ET+CT vs placebo LLLT+ET in AT Kiritsi 2010, LLLT vs placebo LLLT in PF Lamba 2013, LLLT+S vs placebo LLLT+S in PF Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT Stergioulas 2003, LLLT vs placebo LLLT in PT	d lase % CI <u>Mean</u> 40.5 22.6 28.9 40 32	er dos : 14.9 	Se sul 94 to 6 10 17 20 11. 25 40 8 26 18 6	bgrouj 27.31 Control an SD 52 34.37 7.2 17.75 .54 35.09 18 8.9 8.3 53	p and), I ² <u>Total</u> 43 10 21 25 40 26 17	d incr = 0% weight 0.0% 8.2% 8.9% 13.8% 7.6% 11.6% 4.9%	reases the est, $N = 278$) Mean Difference IV, Random, 95% -11.50 [-26.52, 3.5; 5.40 [-16.15, 26.9] 17.36 [-2.36, 37.0] 22.00 [13.31, 30.6] 23.70 [0.47, 46.9] 24.80 [11.21, 38.3] 29.10 [-4.24, 62.4]	stimate of j immediate	placebo-controlle ly after complete Mean Difference
Allocating the study by Darre et a heterogeneity in the recommender reduction to 21.12 mm VAS ((950 therapy (Figure S9). <u>Study or Subgroup</u> 5.1.1 Recommended LLLT dose vs placebo Darre 1994, LLLT vs placebo LLLT in AT Turnilty 2008, LLLT+ET vs placebo LLLT+ET in AT Naterstad, LLLT+ET-CT vs placebo LLLT+ET in AT Kirtisi 2010, LLLT vs placebo LLLT in PF Lamba 2013, LLLT+S vs placebo LLLT+ET in AT Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT Stergioulas 2003, LLLT vs placebo LLLT+ET in AT Stergioulas 2003, LLLT vs placebo LLLT in PT Subtotal (95% C1) Heterogeneity: Tau ² = 0.00; Chi ² = 2.77, df = 5 (P = 0.74); I	d lase % CI <u>Mean</u> 40.5 22.6 28.9 40 32 24.8 35.5	er dos : 14.9 	se sul 94 to 46 10 17 20 11. 25 40 8 26	bgrouj 27.31 control an SD 52 34.37 7.2 17.75 .54 35.09 18 8.9 8.3 53 0 25	p and), I ² <u>Total</u> 43 10 21 25 40 26	d incr = 0% weight 0.0% 8.2% 8.9% 13.8% 7.6% 11.6% 4.9%	reases the est, $N = 278$) Mean Difference IV, Random, 95% -11.50 [-26.52, 3.5; 5.40 [-16.15, 26.9] 17.36 [-2.36, 37.0] 22.00 [13.31, 30.6] 23.70 [0.47, 46.9] 24.80 [11.21, 38.3]	stimate of j immediate	placebo-controlle ly after complete Mean Difference
Allocating the study by Darre et a heterogeneity in the recommender reduction to 21.12 mm VAS ((95% therapy (Figure S9). <u>Study or Subgroup</u> 5.1.1 Recommended LLLT dose vs placebo Darre 1994, LLLT vs placebo LLLT in AT Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT Naterstad, LLLT+ET+CT vs placebo LLLT+ET in AT Kiritsi 2010, LLLT vs placebo LLLT+S in PF Stergioulas 2003, LLLT+S vs placebo LLLT+ET in AT Stergioulas 2003, LLLT vs placebo LLLT in PT Subtotal (95% CI)	d lase % CI <u>Mean</u> 40.5 22.6 28.9 40 32 24.8 35.5	er dos : 14.9 	See sul 94 to 6 10 17 20 11. 25 40 8 26 18 6	bgrouj 27.31 control an SD 52 34.37 7.2 17.75 .54 35.09 18 8.9 8.3 53 0 25	p and), I ² <u>Total</u> 43 10 21 25 40 26 17	d incr = 0% weight 0.0% 8.2% 8.9% 13.8% 7.6% 11.6% 4.9%	reases the est, $N = 278$) Mean Difference IV, Random, 95% -11.50 [-26.52, 3.5; 5.40 [-16.15, 26.9] 17.36 [-2.36, 37.0] 22.00 [13.31, 30.6] 23.70 [0.47, 46.9] 24.80 [11.21, 38.3] 29.10 [-4.24, 62.4]	stimate of j immediate	placebo-controlle ly after complete Mean Difference
Allocating the study by Darre et a heterogeneity in the recommender reduction to 21.12 mm VAS ((95% therapy (Figure S9). <u>Study or Subgroup</u> <u>5.1.1 Recommended LLLT dose vs placebo</u> Dare 1994, LLLT vs placebo LLLT in AT Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT Naterstad, LLLT+ET+CT vs placebo LLLT+ET in AT Naterstad, LLLT+ET+CT vs placebo LLLT+ET in AT Kiritsi 2010, LLLT vs placebo LLLT in PF Lamba 2013, LLLT+S vs placebo LLLT+S in PF Stergioulas 2003, LLLT+ET vs placebo LLLT in PT Subtotal (95% CI) Heterogeneity: Tau ² = 0.00; Chi ² = 2.77, df = 5 (P = 0.74); I Test for overall effect: Z = 6.69 (P < 0.00001) 5.1.2 Non-recommended LLLT dose vs placebo	d lase % CI <u>Mean</u> 40.5 22.6 28.9 40 32 24.8 35.5 ² = 0%	er dos : 14.9 	se sul 94 to 10 17 20 11. 25 40 8 26 18 6 139	bgrouj 27.31 an SD 52 34.37 7.2 17.75 54 35.09 18 8.9 8.3 53 0 25 6.4 12.39	p and), I ² <u>Total</u> 43 10 21 25 40 26 17 139	d incr = 0% weight 0.0% 8.2% 8.9% 13.8% 7.6% 13.8% 7.6% 14.8%	reases the est, $N = 278$) Mean Difference IV, Random, 95% -11.50 [-26.52, 3.5; 5.40 [-16.15, 26.9] 17.36 [-2.36, 37.0 22.00 [13.31, 30.6 23.70 [0.47, 46.9] 24.80 [11.21, 38.3 29.10 [-4.24, 62.4, 21.12 [14.94, 27.31]	stimate of j immediate	placebo-controlle ly after complete Mean Difference
Allocating the study by Darre et a heterogeneity in the recommender reduction to 21.12 mm VAS ((95% therapy (Figure S9). <u>Study or Subgroup</u> 5.1.1 Recommended LLLT dose vs placebo Darre 1994, LLLT vs placebo LLLT in AT Tumity 2008, LLLT+ET vs placebo LLLT+ET in AT Naterstad, LLLT+ET+CT vs placebo LLLT+ET in AT Kirtisi 2010, LLLT vs placebo LLLT in PF Lamba 2013, LLLT+S vs placebo LLLT+ET in AT Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT Stergioulas 2003, LLLT vs placebo LLLT in PF Subtotal (95% CI) 5.1.2 Non-recommended LLLT dose vs placebo Tumity 2012, LLLT+ET vs placebo LLLT+ET in AT Subtotal (95% CI)	d lase % CI <u>Mean</u> 40.5 22.6 28.9 40 32 24.8 35.5 ² = 0%	er dos : 14.9 	See sul 94 to 6 10 17 20 11. 25 40 8 26 18 6	bgrouj 27.31 control an SD 52 34.37 7.2 17.75 .54 35.09 18 8.9 8.3 53 0 25	p and), I ² Total 43 10 21 25 40 26 17 139	d incr = 0% weight 0.0% 8.2% 8.9% 13.8% 7.6% 11.6% 4.9%	reases the est, $N = 278$) Mean Difference IV, Random, 95% -11.50 [-26.52, 3.5; 5.40 [-16.15, 26.9] 17.36 [-2.36, 37.0] 22.00 [13.31, 30.6] 23.70 [0.47, 46.9] 24.80 [11.21, 38.3] 29.10 [-4.24, 62.4]	stimate of j immediate	placebo-controlle ly after complete Mean Difference
Allocating the study by Darre et a heterogeneity in the recommender reduction to 21.12 mm VAS ((95% therapy (Figure S9). <u>Study or Subgroup</u> <u>5.1.1 Recommended LLLT dose vs placebo</u> Darre 1994, LLLT vs placebo LLLT in AT Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT Naterstad, LLLT+ET+CT vs placebo LLLT+ET in AT Kiritsi 2010, LLLT vs placebo LLLT in PF Lamba 2013, LLLT+S vs placebo LLLT+ET in AT Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT Stergioulas 2008, LLLT+ET vs placebo LLLT in PF Stergioulas 2003, LLLT vs placebo LLLT in PT Subtotal (95% CI) Heterogeneity: Tau ² = 0.00; Chi ² = 2.77, df = 5 (P = 0.74); I Test for overall effect: Z = 6.69 (P < 0.00001) <u>5.1.2 Non-recommended LLLT dose vs placebo</u> Tumilty 2012, LLLT+ET vs placebo LLLT+ET in AT Subtotal (95% CI) Heterogeneity: Not applicable	d lase % CI <u>Mean</u> 40.5 22.6 28.9 40 32 24.8 35.5 ² = 0%	er dos : 14.9 	se sul 94 to 10 17 20 11. 25 40 8 26 18 6 139	bgrouj 27.31 an SD 52 34.37 7.2 17.75 54 35.09 18 8.9 8.3 53 0 25 6.4 12.39	p and), I ² Total 43 10 21 25 40 26 17 139	d incr = 0% <u>Weight</u> 0.0% 8.9% 13.8% 7.6% 11.6% 4.9% 54.8%	reases the est, $N = 278$) Mean Difference IV, Random, 95% -11.50 [-26.52, 3.5; 5.40 [-16.15, 26.9; 17.36 [-2.36, 37.0; 22.00 [13.31, 30.6; 23.70 [0.47, 46.9; 24.80 [11.21, 38.3; 29.10 [-4.24, 62.4; 21.12 [14.94, 27.31] -3.00 [-11.17, 5.1]	stimate of j immediate	placebo-controlle ly after complete Mean Difference
Allocating the study by Darre et a heterogeneity in the recommender reduction to 21.12 mm VAS ((95% therapy (Figure S9). <u>Study or Subgroup</u> 5.1.1 Recommended LLLT dose vs placebo Darre 1994, LLLT vs placebo LLLT in AT Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT Naterstad, LLLT+ET-CT vs placebo LLLT+ET in AT Naterstad, LLLT+ET vs placebo LLLT+ET in AT Stergioulas 2008, LLLT vs placebo LLLT in PT Subtoal (95% C1) Heterogeneity: Tau ² = 0.00; Chi ² = 2.77, df = 5 (P = 0.74); I Test for overall effect: Z = 6.69 (P < 0.00001) 5.1.2 Non-recommended LLLT dose vs placebo Tumilty 2012, LLLT+ET vs placebo LLLT+ET in AT Subtoal (95% C1) Heterogeneity: Not applicable Test for overall effect: Z = 0.72 (P = 0.47)	d lase % CI <u>Mean</u> 40.5 22.6 28.9 40 32 24.8 35.5 ² = 0%	er dos : 14.9 	se sul 94 to 10 17 20 11. 25 40 8 26 18 6 139	bgrouj 27.31 an SD 52 34.37 7.2 17.75 54 35.09 18 8.9 8.3 53 0 25 6.4 12.39	p and), I ² Total 43 10 21 25 40 26 17 139	d incr = 0% <u>Weight</u> 0.0% 8.9% 13.8% 7.6% 11.6% 4.9% 54.8%	reases the est, $N = 278$) Mean Difference IV, Random, 95% -11.50 [-26.52, 3.5; 5.40 [-16.15, 26.9; 17.36 [-2.36, 37.0; 22.00 [13.31, 30.6; 23.70 [0.47, 46.9; 24.80 [11.21, 38.3; 29.10 [-4.24, 62.4; 21.12 [14.94, 27.31] -3.00 [-11.17, 5.1]	stimate of j immediate	placebo-controlle ly after complete Mean Difference
Allocating the study by Darre et a heterogeneity in the recommender reduction to 21.12 mm VAS ((95% therapy (Figure S9). <u>Study or Subgroup</u> <u>5.1.1 Recommended LLLT dose vs placebo</u> Darre 1994, LLLT vs placebo LLLT in AT Tumity 2008, LLLT+ET vs placebo LLLT+ET in AT Naterstad, LLLT+ET+CT vs placebo LLLT+ET in AT Kirtsi 2010, LLLT vs placebo LLLT+S in PF Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT Stergioulas 2008, LLLT+ET vs placebo LLLT in PF Subtotal (95% CI) Heterogeneity: Tau ² = 0.00; Chi ² = 2.77, df = 5 (P = 0.74); I Test for overall effect: Z = 6.69 (P < 0.00001) 5.1.2 Non-recommended LLLT dose vs placebo Tumity 2012, LLLT+ET vs placebo LLLT+ET in AT Subtotal (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.72 (P = 0.47) 5.1.3 Unknown LLLT dose vs placebo Darre 1994, LLLT vs placebo LLLT in AT	d lase % CI <u>L</u> 40.5 22.6 28.9 40 32 24.8 35.5 1 ² = 0% 6	er dos : 14.9 	se sul 94 to 10 17 20 11. 25 40 8 26 18 6 139 20 20 20 46	bgrOu 27.31 Control an SD 52 34.37 7.2 17.75 54 35.09 18 8.9 18 8.9 17 75 52 34.37 75 55 54 35.09 18 8.9 18 8.9 1	p an.), I ² <u>Total</u> 43 100 21 25 40 26 17 139 20 20 43	d incr = 0% <u>Weight</u> 0.0% 8.2% 13.8% 7.6% 11.6% 4.9% 54.8% 14.0% 14.0%	reases the est, $N = 278$) Mean Difference IV, Random, 95% -11.50 [-26.52, 3.5; 5.40 [-16.15, 26.9; 17.36 [-2.36, 37.0) 22.00 [13.31, 30.6; 23.70 [0.47, 46.9; 24.80 [11.21, 38.3; 29.10 [-4.24, 62.4; 21.12 [14.94, 27.31] -3.00 [-11.17, 5.1] -3.00 [-11.17, 5.1] -11.50 [-26.52, 3.5]	stimate of j immediate	placebo-controlle ly after complete Mean Difference
Allocating the study by Darre et a heterogeneity in the recommender reduction to 21.12 mm VAS ((95% therapy (Figure S9). <u>Study or Subgroup</u> <u>5.1.1 Recommended LLLT dose vs placebo</u> Dare 1994, LLLT vs placebo LLLT in AT Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT Naterstad, LLLT+ET+CT vs placebo LLLT+ET in AT Naterstad, LLLT+ET+CT vs placebo LLLT+ET in AT Kiritsi 2010, LLLT vs placebo LLLT in PF Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT Stergioulas 2008, LLLT+ET vs placebo LLLT in PF Subtotal (95% CI) Heterogeneity: Tau ² = 0.00; Chi ² = 2.77, df = 5 (P = 0.74); I Test for overall effect: Z = 6.69 (P < 0.00001) 5.1.2 Non-recommended LLLT dose vs placebo Tumilty 2012, LLLT+ET vs placebo LLLT+ET in AT Subtotal (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.72 (P = 0.47) 5.1.3 Unknown LLLT dose vs placebo Darre 1994, LLLT vs placebo LLLT in AT Basford 1998, LLLT vs placebo LLLT in PF	d lase % CI <u>Mean</u> 40.5 22.6 28.9 40 32 24.8 35.5 ² = 0% 6	er dos : 14.9 	se sul 94 to 10 17 20 11. 25 40 8 26 18 6 139 20 20 46 16 26	bgrouj 27.31 control an SD 52 34.37 7.2 17.75 54 35.09 18 8.9 8.3 53 0 25 6.4 12.39 9 7.45 52 34.37 6.1 29.26	p an- p an- <u>Total</u> 43 10 21 25 40 26 26 20 20	d incr = 0% weight 0.0% 8.2% 8.9% 13.8% 7.6% 11.6% 4.9% 54.8% 14.0% 14.0%	eases the est, $N = 278$) Mean Difference IV, Random, 95% -11.50 [-26.52, 3.5; 5.40 [-16.15, 26.9] 17.36 [-2.36, 37.0] 22.00 [13.31, 30.6] 23.70 [0.47, 46.9] 24.80 [11.21, 38.3] 29.10 [-4.24, 62.4] 21.12 [14.94, 27.31] -3.00 [-11.17, 5.1] -3.00 [-11.17, 5.1] -11.50 [-26.52, 3.5; 8.30 [-18.50, 35.1]	zi mate of j immediate	placebo-controlle ly after complete Mean Difference
Allocating the study by Darre et a heterogeneity in the recommender reduction to 21.12 mm VAS ((95% therapy (Figure S9). <u>Study or Subgroup</u> 5.1.1 Recommended LLLT dose vs placebo Darre 1994, LLLT vs placebo LLLT in AT Tumity 2008, LLLT+ET vs placebo LLLT+ET in AT Naterstad, LLLT+ET-CT vs placebo LLLT+ET in AT Kirtisi 2010, LLLT vs placebo LLLT +ET in AT Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT Stergioulas 2008, LLLT vs placebo LLLT in PF Stergioulas 2008, LLLT vs placebo LLLT +ET in AT Stergioulas 2008, LLLT vs placebo LLLT in PT Subtotal (95% CI) Heterogeneity: Tau ² = 0.00; Chi ² = 2.77, df = 5 (P = 0.74); I Test for overall effect: Z = 6.69 (P < 0.00001) 5.1.2 Non-recommended LLLT dose vs placebo Tumilty 2012, LLLT+ET vs placebo LLLT +ET in AT Subtotal (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.72 (P = 0.47) 5.1.3 Unknown LLLT dose vs placebo Darre 1994, LLLT vs placebo LLLT in AT Basford 1998, LLLT vs placebo LLLT in PF Macias 2015, LLLT vs placebo LLLT in PF Subtotal (95% CI)	d lase % CI <u>Mean</u> 40.5 22.6 28.9 40 32 24.8 35.5 I ² = 0% 6 40.5 34.4 19.8	er dos : 14.9 	se sul 94 to 10 17 20 11. 25 40 8 26 18 6 139 20 20 46 16 26	bgrOu 27.31 Control an SD 52 34.37 7.2 17.75 54 35.09 18 8.9 18 8.9 17 75 52 34.37 75 55 54 35.09 18 8.9 18 8.9 1	p an- p an- <u>Total</u> 43 10 21 25 40 26 26 20 20	d incr = 0% <u>Weight</u> 0.0% 8.2% 13.8% 7.6% 11.6% 4.9% 54.8% 14.0% 14.0%	reases the est, $N = 278$) Mean Difference IV, Random, 95% -11.50 [-26.52, 3.5; 5.40 [-16.15, 26.9; 17.36 [-2.36, 37.0) 22.00 [13.31, 30.6; 23.70 [0.47, 46.9; 24.80 [11.21, 38.3; 29.10 [-4.24, 62.4; 21.12 [14.94, 27.31] -3.00 [-11.17, 5.1] -3.00 [-11.17, 5.1] -11.50 [-26.52, 3.5]	zi mate of j immediate	placebo-controlle ly after complete Mean Difference
Allocating the study by Darre et a heterogeneity in the recommender reduction to 21.12 mm VAS ((95% therapy (Figure S9). <u>Study or Subgroup</u> <u>5.1.1 Recommended LLLT dose vs placebo</u> Dare 1994, LLLT vs placebo LLLT in AT Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT Naterstad, LLLT+ET+CT vs placebo LLLT+ET in AT Naterstad, LLLT+S vs placebo LLLT in PF Stergioulas 2008, LLLT+ET vs placebo LLLT+S in PF Stergioulas 2003, LLLT+S vs placebo LLLT in PT Subtotal (95% CI) Heterogeneity: Tau ² = 0.00; Chi ² = 2.77, df = 5 (P = 0.74); I Test for overall effect: Z = 6.69 (P < 0.00001) <u>5.1.2 Non-recommended LLLT dose vs placebo</u> Tumilty 2012, LLLT+ET vs placebo LLLT+ET in AT Subtotal (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.72 (P = 0.47) <u>5.1.3 Unknown LLLT dose vs placebo</u> Darre 1994, LLLT vs placebo LLLT in AT Basford 1998, LLLT vs placebo LLLT in PF Macias 2015, LLLT vs placebo LLLT in PF	d lase % CI <u>Mean</u> 40.5 22.6 28.9 40 32 24.8 35.5 I ² = 0% 6 40.5 34.4 19.8	er dos : 14.9 	Se sul 24 to 24 to 46 10 17 20 11 25 40 8 26 18 6 139 20 20 20 20 20 20 20 20 20 20	bgrouj 27.31 control an SD 52 34.37 7.2 17.75 54 35.09 18 8.9 8.3 53 0 25 6.4 12.39 9 7.45 52 34.37 6.1 29.26	p and), I ² <u>Total</u> 43 10 21 25 40 26 17 139 20 20 20 43 15 32	d incr = 0% weight 0.0% 8.2% 8.9% 13.8% 7.6% 13.8% 7.6% 14.0% 14.0% 14.0% 14.0%	reases the est, $N = 278$) Mean Difference IV, Random, 95% -11.50 [-26.52, 3.5; 5.40 [-16.15, 26.9] 17.36 [-2.36, 37.0] 22.00 [13.31, 30.6] 23.70 [0.47, 46.9] 24.80 [11.21, 38.3] 29.10 [-4.24, 62.4] -3.00 [-11.17, 5.1] -3.00 [-11.17, 5.1] -3.00 [-11.17, 5.1] -11.50 [-26.52, 3.5; 8.30 [-18.50, 35.1] 11.10 [2.27, 19.9]	zi mate of j immediate	placebo-controlle ly after complete Mean Difference
Allocating the study by Darre et a heterogeneity in the recommender reduction to 21.12 mm VAS ((95% therapy (Figure S9). <u>Study or Subgroup</u> <u>5.1.1 Recommended LLLT dose vs placebo</u> Dare 1994, LLLT vs placebo LLLT in AT Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT Naterstad, LLLT+ET+CT vs placebo LLLT+ET in AT Naterstad, LLLT+ET+CT vs placebo LLLT+ET in AT Kiritsi 2010, LLLT vs placebo LLLT in PF Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT Stergioulas 2008, LLLT+ET vs placebo LLLT in PF Subtotal (95% CI) Heterogeneity: Tau ² = 0.00; Chi ² = 2.77, df = 5 (P = 0.74); I Test for overall effect: Z = 6.69 (P < 0.00001) <u>51.2 Non-recommended LLLT dose vs placebo</u> Tumilty 2012, LLLT+ET vs placebo LLLT+ET in AT Subtotal (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.72 (P = 0.47) <u>51.3 Unknown LLLT dose vs placebo</u> Darre 1994, LLLT vs placebo LLLT in PF Macias 2015, LLLT vs placebo LLLT in PF Macias 2015, LLLT vs placebo LLLT in PF Subtotal (95% CI) Heterogeneity: Tau ² = 135.31; Chi ² = 6.51, df = 2 (P = 0.04 Test for overall effect: Z = 0.31 (P = 0.75)	d lase % CI <u>Mean</u> 40.5 22.6 28.9 40 32 24.8 35.5 I ² = 0% 6 40.5 34.4 19.8	er dos : 14.9 : 14.9 : 14.9 : 14.9 : 14.9 : 14.9 : 14.9 : 17.9 : 17.1 : 17.1 : 17.1 : 17.1 : 17.1 : 17.1 : 17.1 : 17.9 : 17.9 : 14.9 : 14.9	Se sul 24 to 24 to 46 10 17 20 11 25 40 8 26 18 6 139 20 20 20 20 20 20 20 20 20 20	bgrouj 27.31 control an SD 52 34.37 7.2 17.75 54 35.09 18 8.9 8.3 53 0 25 6.4 12.39 9 7.45 52 34.37 6.1 29.26	p an. <u>Total</u> <u>10</u> 21 25 40 26 17 139 20 20 20 43 15 32 90	d incr = 0% weight 0.0% 8.2% 8.9% 13.8% 7.6% 13.8% 7.6% 14.0% 14.0% 14.0% 14.0%	reases the est, $N = 278$) Mean Difference IV, Random, 95% -11.50 [-26.52, 3.5; 5.40 [-16.15, 26.9] 17.36 [-2.36, 37.0] 22.00 [13.31, 30.6] 23.70 [0.47, 46.9] 24.80 [11.21, 38.3] 29.10 [-4.24, 62.4] -3.00 [-11.17, 5.1] -3.00 [-11.17, 5.1] -3.00 [-11.17, 5.1] -3.00 [-11.17, 5.1] -3.00 [-11.17, 5.1] -11.50 [-26.52, 3.5; 8.30 [-18.50, 35.1] 11.10 [2.27, 19.9] 2.58 [-13.60, 18.76]	zi mate of j immediate	placebo-controlle ly after complete Mean Difference
Allocating the study by Darre et a heterogeneity in the recommender reduction to 21.12 mm VAS ((95% therapy (Figure S9). <u>Study or Subgroup</u> 5.1.1 Recommended LLLT dose vs placebo Darre 1994, LLLT vs placebo LLLT in AT Tumity 2008, LLLT+ET vs placebo LLLT+ET in AT Naterstad, LLLT+ET+CT vs placebo LLLT+ET in AT Naterstad, LLLT+ET+CT vs placebo LLLT+ET in AT Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT Stergioulas 2003, LLLT vs placebo LLLT in PT Subtotal (95% CI) Heterogeneity: Tau ² = 0.00; Chi ² = 2.77, df = 5 (P = 0.74); I Test for overall effect: Z = 6.69 (P < 0.00001) 5.1.2 Non-recommended LLLT dose vs placebo Tumity 2012, LLLT+ET vs placebo LLLT+ET in AT Subtotal (95% CI) Heterogeneity: Not applicable Test for overall effect: Z = 0.72 (P = 0.47) 5.1.3 Unknown LLLT dose vs placebo Darre 1994, LLLT vs placebo LLLT in AT Basford 1998, LLLT vs placebo LLLT in PF Macias 2015, LLLT vs placebo LLLT in PF	d lase % CI 40.5 22.6 28.9 40 32 24.8 35.5 1 ² = 0% 6 40.5 34.4 19.8	er dos : 14.9 	se sul 94 to 10 11 20 11. 25 40 4 26 13 18 6 139 20 20 20 20 46 16 26 37 8 99	bgrouj 27.31 control an SD 52 34.37 7.2 17.75 54 35.09 18 8.9 8.3 53 0 25 6.4 12.39 9 7.45 52 34.37 6.1 29.26	p an. <u>Total</u> <u>10</u> 21 25 40 26 17 139 20 20 20 43 15 32 90	d incr = 0% weight 0.0% 8.2% 8.9% 13.8% 7.6% 13.8% 7.6% 13.8% 54.8% 14.0% 14.0% 14.0% 14.0% 14.0% 14.0%	reases the est, $N = 278$) Mean Difference IV, Random, 95% -11.50 [-26.52, 3.5; 5.40 [-16.15, 26.9] 17.36 [-2.36, 37.0] 22.00 [13.31, 30.6] 23.70 [0.47, 46.9] 24.80 [11.21, 38.3] 29.10 [-4.24, 62.4] -3.00 [-11.17, 5.1] -3.00 [-11.17, 5.1] -3.00 [-11.17, 5.1] -11.50 [-26.52, 3.5; 8.30 [-18.50, 35.1] 11.10 [2.27, 19.9]	zi mate of j immediate	placebo-controlle ly after complete Mean Difference

AT, Achilles tendinopathy; CT, cryotherapy; ET, exercise therapy; LLLT, Low-Level Laser Therapy; PF,
 plantar fasciitis; PT, patellar tendinopathy; S, stretching.

Risk-of-bias within studies post-hoc analyses

2			LLLT		c	Control			Mean Difference	Mean Difference
3	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4	17.1.1 Blinded assessor									
	Tumilty 2012, LLLT+ET vs placebo LLLT+ET in AT	6	17.1	20	9	7.45	20	21.1%	-3.00 [-11.17, 5.17]	
5	Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT	22.6	29.9	10	17.2	17.75	10	11.0%	5.40 [-16.15, 26.95]	
6	Basford 1998, LLLT vs placebo LLLT in PF			16	26.1	29.26	15	8.4%	8.30 [-18.50, 35.10]	
-	Macias 2015, LLLT vs placebo LLLT in PF			37	8.7	14.56	32	20.6%	11.10 [2.27, 19.93]	
/	Naterstad, LLLT+ET+CT vs placebo LLLT+ET+CT in AT				11.54	35.09	21	12.1%	17.36 [-2.36, 37.08]	-
8	Kiritsi 2010, LLLT vs placebo LLLT in PF	40	20.3	25	18	8.9	25	20.7%	22.00 [13.31, 30.69]	
	Stergioulas 2003, LLLT vs placebo LLLT in PT Subtotal (95% CI)	35.5	71.04	18 146	6.4	12.39	17 140	6.2% 100.0%	29.10 [-4.24, 62.44]	
9		A). 12 - 1	200/	140			140	100.076	11.38 [1.85, 20.91]	
10	Heterogeneity: Tau ² = 94.57; Chi ² = 19.09, df = 6 (P = 0.00) Test for overall effect: $Z = 2.34$ (P = 0.02)	/4); I [~] = 6	59%							
11	Test for overall effect. $2 - 2.34$ (F - 0.02)									
	17.1.3 Un-blinded assessor									
12	Darre 1994, LLLT vs placebo LLLT in AT	40.5	37.91	46	52	34.37	43	34.8%	-11.50 [-26.52, 3.52]	
13	Lamba 2013, LLLT+S vs placebo LLLT+S in PF	32	53	40	8.3	53	40	29.7%	23.70 [0.47, 46.93]	
	Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT	24.8	25	26	0	25	26	35.5%	• • •	
14	Subtotal (95% CI)			112			109	100.0%	11.86 [-13.50, 37.21]	
15	Heterogeneity: Tau ² = 422.80; Chi ² = 13.73, df = 2 (P = 0.0	01); l² =	85%							
16	Test for overall effect: Z = 0.92 (P = 0.36)									
17									-	-50 -25 0 25 50
18										Favours placebo Favours LLLT
10	Test for subgroup differences: Chi ² = 0.00, df = 1 (P = 0.97), $ ^2 = 0^{\circ}$	6							

Figure S10: Blinded versus unblinded assessor

AT, Achilles tendinopathy; CT, cryotherapy; ET, exercise therapy; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S, stretching.

24										
25										
26			LLLT		c	Control			Mean Difference	Mean Difference
27	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
28	19.1.1 Blinded therapist									
	Darre 1994, LLLT vs placebo LLLT in AT		37.91	46		34.37	43	19.9%		
29	Tumilty 2012, LLLT+ET vs placebo LLLT+ET in AT	6	17.1	20	9	7.45	20	23.6%	-3.00 [-11.17, 5.17]	
30	Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT	22.6	29.9	10	17.2		10	16.1%	5.40 [-16.15, 26.95]	
31	Naterstad, LLLT+ET+CT vs placebo LLLT+ET+CT in AT Kiritsi 2010, LLLT vs placebo LLLT in PF	28.9 40	29.18 20.3	20 25	11.54 18	35.09 8.9	21 25	17.1% 23.4%	17.36 [-2.36, 37.08] 22.00 [13.31, 30.69]	
	Subtotal (95% CI)	40	20.5	121	10	0.9	119	100.0%	5.98 [-8.14, 20.10]	
32	Heterogeneity: Tau ² = 202.36; Chi ² = 24.10, df = 4 (P < 0.0	0001)· l²	= 83%							
33	Test for overall effect: $Z = 0.83$ (P = 0.41)		0070							
34										
	19.1.3 Un-blinded therapist									
35	Basford 1998, LLLT vs placebo LLLT in PF	34.4	45.58	16	26.1	29.26	15	6.6%	8.30 [-18.50, 35.10]	<u> </u>
36	Macias 2015, LLLT vs placebo LLLT in PF		22.49	37	8.7	14.56	32	55.3%	11.10 [2.27, 19.93]	
37	Lamba 2013, LLLT+S vs placebo LLLT+S in PF	32	53	40	8.3	53	40	8.8%	23.70 [0.47, 46.93]	
	Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT	24.8	25	26	0	25	26	24.9%	24.80 [11.21, 38.39]	
38	Stergioulas 2003, LLLT vs placebo LLLT in PT Subtotal (95% CI)	35.5	71.04	18 137	6.4	12.39	17 130	4.3% 100.0%	29.10 [-4.24, 62.44] 16.21 [9.26, 23.16]	
39	Heterogeneity: Tau ² = 2.44; Chi ² = 4.13, df = 4 (P = 0.39);	1 ² = 3%		157			150	100.078	10.21 [3.20, 23.10]	•
40	Test for overall effect: $Z = 4.57$ (P < 0.00001)	1 = 0 /0								
41									-	
42										-50 -25 0 25 50 Favours placebo Favours LLLT
43	Test for subgroup differences: Chi ² = 1.62, df = 1 (P = 0.20), I² = 38	3.4%							
-5										

Figure S11: Blinded versus unblinded therapist

AT, Achilles tendinopathy; CT, cryotherapy; ET, exercise therapy; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S, stretching.

2

3

4

26

27

28

29 30

BMJ Open

Risk-of-bias across studies - random versus fixed effects meta-analysis results of pain

There was almost no difference between the pain point estimates of the random and fixed effects models (pain immediately after the end of therapy), that is, 11.48 mm versus 10.21 mm VAS, indicating that no small study bias exists (Figures S12 and S13).

5			LLLT		0	ontrol			Mean Difference	Mean Difference
6	Study or Subgroup	Mean		Total	-		Total	Weight		
7	5.1.1 Recommended LLLT dose vs placebo									
,	Darre 1994, LLLT vs placebo LLLT in AT		37.91	46		34.37	43	10.9%	-11.50 [-26.52, 3.52]	
8	Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT	22.6	29.9	10		17.75	10	8.2%	5.40 [-16.15, 26.95]	
9	Naterstad, LLLT+ET+CT vs placebo LLLT+ET+CT in AT	28.9			11.54		21	8.9%	17.36 [-2.36, 37.08]	
10	Kiritsi 2010, LLLT vs placebo LLLT in PF	40	20.3 53	25 40	18	8.9	25 40	13.8%	22.00 [13.31, 30.69]	
	Lamba 2013, LLLT+S vs placebo LLLT+S in PF Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT	32 24.8	25	40 26	8.3 0	53 25	40 26	7.6% 11.6%	23.70 [0.47, 46.93] 24.80 [11.21, 38.39]	
11	Stergioulas 2003, LLLT vs placebo LLLT in PT		71.04	18	-	12.39	17	4.9%	29.10 [-4.24, 62.44]	
12	Subtotal (95% CI)	00.0	71.04	185	0.4	12.00	182	65.7%	14.98 [3.74, 26.22]	◆
13	Heterogeneity: Tau ² = 140.53; Chi ² = 18.27, df = 6 (P = 0.0	06); l² =	67%							
	Test for overall effect: Z = 2.61 (P = 0.009)									
14										
15	5.1.2 Non-recommended LLLT dose vs placebo									
16	Tumilty 2012, LLLT+ET vs placebo LLLT+ET in AT Subtotal (95% CI)	6	17.1	20 20	9	7.45	20 20	14.0% 14.0%	-3.00 [-11.17, 5.17] -3.00 [-11.17, 5.17]	•
17	Heterogeneity: Not applicable									
	Test for overall effect: Z = 0.72 (P = 0.47)									
18	5.1.3 Unknown LLLT dose vs placebo									
19			45 50	40	00.4	00.00	45	0 40/	0.001.40.50.05.401	
20	Basford 1998, LLLT vs placebo LLLT in PF Macias 2015, LLLT vs placebo LLLT in PF		45.58 22.49	16 37		29.26 14.56	15 32	6.4% 13.8%	8.30 [-18.50, 35.10] 11.10 [2.27, 19.93]	
	Subtotal (95% CI)	19.0	22.49	53	0.7	14.50	47	20.2%	10.83 [2.44, 19.21]	•
21	Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.04$, $df = 1$ (P = 0.85);	$ ^2 = 0\%$								•
22	Test for overall effect: $Z = 2.53$ (P = 0.01)									
23	Total (95% CI)			258			240	100.0%	14 49 53 69 30 301	
		0011-12	- 720/	200			249	100.0%	11.48 [2.68, 20.28]	
24	Heterogeneity: $Tau^2 = 126.14$; $Chi^2 = 32.84$, $df = 9$ (P = 0.0 Test for overall effect: Z = 2.56 (P = 0.01)	(001); I-	= 73%							-100 -50 0 50 100
25	Test for subgroup differences: $Chi^2 = 8.38$, df = 2 (P = 0.02)	?), l² = 76	5.1%							Favours placebo Favours LLLT

Figure S12: Random effects meta-analysis model

AT, Achilles tendinopathy; CT, cryotherapy; ET, exercise therapy; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S, stretching.

31												
32												
33			LLLT		c	Control			Mean Difference		Mean Difference	
	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% C	I	IV, Fixed, 95% CI	
34	5.1.1 Recommended LLLT dose vs placebo											
35	Darre 1994, LLLT vs placebo LLLT in AT		37.91	46		34.37	43		-11.50 [-26.52, 3.52]			
	Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT	22.6	29.9	10		17.75	10	3.6%				
36	Naterstad, LLLT+ET+CT vs placebo LLLT+ET+CT in AT	28.9	29.18		11.54		21		17.36 [-2.36, 37.08]			
37	Kiritsi 2010, LLLT vs placebo LLLT in PF	40	20.3	25	18	8.9	25	22.2%	22.00 [13.31, 30.69]			
	Lamba 2013, LLLT+S vs placebo LLLT+S in PF	32	53	40	8.3	53	40	3.1%	23.70 [0.47, 46.93]			
38	Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT	24.8	25	26	0	25	26	9.1%	24.80 [11.21, 38.39]			
39	Stergioulas 2003, LLLT vs placebo LLLT in PT Subtotal (95% CI)	35.5	71.04	18 185	6.4	12.39	17 182		29.10 [-4.24, 62.44] 16.39 [10.67, 22.11]		•	
40	Heterogeneity: Chi ² = 18.27, df = 6 (P = 0.006); l ² = 67%											
41	Test for overall effect: Z = 5.62 (P < 0.00001)											
42	5.1.2 Non-recommended LLLT dose vs placebo											
43	Tumilty 2012, LLLT+ET vs placebo LLLT+ET in AT Subtotal (95% CI)	6	17.1	20 20	9	7.45	20 20	25.0% 25.0%	-3.00 [-11.17, 5.17] -3.00 [-11.17, 5.17]		•	
44	Heterogeneity: Not applicable											
45	Test for overall effect: Z = 0.72 (P = 0.47)											
46	5.1.3 Unknown LLLT dose vs placebo											
47	Basford 1998, LLLT vs placebo LLLT in PF	34.4	45.58	16	26.1	29.26	15	2.3%	8.30 [-18.50, 35.10]			
	Macias 2015, LLLT vs placebo LLLT in PF	19.8	22.49	37	8.7	14.56	32	21.5%	11.10 [2.27, 19.93]			
48	Subtotal (95% CI)			53			47	23.8%	10.83 [2.44, 19.21]		◆	
49	Heterogeneity: Chi ² = 0.04, df = 1 (P = 0.85); I ² = 0%											
	Test for overall effect: Z = 2.53 (P = 0.01)											
50				050			0.40	100.00/	40.04.00.40.44.001			
51	Total (95% CI)			258			249	100.0%	10.21 [6.12, 14.30]			
	Heterogeneity: Chi ² = 32.84, df = 9 (P = 0.0001); l ² = 73%									-100	-50 0 50	100
52	Test for overall effect: Z = 4.89 (P < 0.00001)										Favours placebo Favours LLLT	
53	Test for subgroup differences: $Chi^2 = 14.54$, df = 2 (P = 0.0	1007), l²	= 86.2%	6								

54 Figure S13: Fixed effects meta-analysis model

AT, Achilles tendinopathy; CT, cryotherapy; ET, exercise therapy; LLLT, Low-Level Laser Therapy; PF,
 plantar fasciitis; PT, patellar tendinopathy; S, stretching.

Risk-of-bias between studies - funnel plot

Funnel plot of pain results immediately after completed therapy indicating that publication bias is absent (Figure S14).

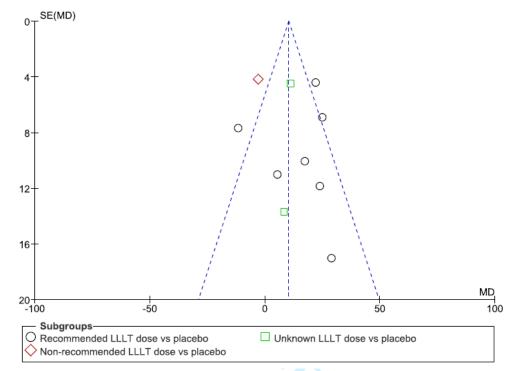


Figure S14: Funnel plot

LLLT, Low-Level Laser Therapy; MD, mean difference; SE, standard error.

References

- Abat F, Sánchez-Sánchez JL, Martín-Nogueras AM, et al. Randomized controlled trial comparing the effectiveness of the ultrasound-guided galvanic electrolysis technique (USGET) versus conventional electro-physiotherapeutic treatment on patellar tendinopathy. *J Exp Orthop* 2016;3(1):34. doi: 10.1186/s40634-016-0070-4 [published Online First: 2016/11/18]
- 2. Aigner N, Fialka C, Weinstabl R, et al. Laser acupuncture for patellar tendinitis in athletes. [German]. *Akupunktur* 1996;24(1):11-14.
- 3. Ashok N, Raghul, S., Sivakumar, V.P.R. Compare The Effects of Low-Level Laser and Ultrasonic Therapy in Subjects with Jumper's Knee. *International Journal of Research and Scientific Innovation* 2018;V(I)
- 4. Atik OS. Photobiomodulation for Achilles Tendinopathy. *Photomedicine and laser surgery* 2018;36(1):12. doi: <u>http://dx.doi.org/10.1089/pho.2017.4361</u>
- 5. Bjordal JM, Lopes-Martins RA, Iversen VV. A randomised, placebo controlled trial of low level laser
 therapy for activated Achilles tendinitis with microdialysis measurement of peritendinous
 prostaglandin E2 concentrations. *Br J Sports Med* 2006;40(1):76-80; discussion 76-80. doi:
 10.1136/bjsm.2005.020842 [published Online First: 2005/12/24]
- 6. Chang YP, Chiang H, Shih KS, et al. Effects of Therapeutic Physical Agents on Achilles Tendon
 Microcirculation. *J Orthop Sports Phys Ther* 2015;45(7):563-9. doi: 10.2519/jospt.2015.5681
 [published Online First: 2015/06/04]
- 7. Cinar E, Uygur F. Extracorporeal shock wave therapy versus low intensity laser therapy in the treatment of heel pain. Annals of the Rheumatic Diseases Conference: Annual European Congress of Rheumatology of the European League Against Rheumatism, EULAR 2013;72(no pagination) doi: http://dx.doi.org/10.1136/annrheumdis-2013-eular.1709
- 8. Cinar E, Uygur F, Toprak Celenay S. The efficacy of low level laser therapy in the treatment of calcaneal
 spur. Annals of the Rheumatic Disease Conference: Annual European Congress of Rheumatology of

Page 37 of 39

BMJ Open

1	the European League Against Rheumatism, EULAR 2012;71(no pagination) doi:
1 2	http://dx.doi.org/10.1136/annrheumdis-2012-eular.1438
3	9. Costantino C, Pogliacomi F, Vaienti E. Cryoultrasound therapy and tendonitis in athletes: a comparative
4	evaluation versus laser CO2 and t.e.ca.r. therapy. Acta Biomed 2005;76(1):37-41. [published Online
5	First: 2005/08/25]
6	10. Coughlin M, Stevens F, Doty J, et al. Evaluation of low-level laser therapy at 635nm for the treatment of
7	chronic plantar fasciitis: A placebo-controlled, randomized study. Lasers in surgery and medicine
8	2014;46:53-54. doi: http://dx.doi.org/10.1002/lsm.22229
9	11. Fernandes MS, Correia MG, Carvalho ML, et al. Laser therapy of inflammatory lesions of the soft parts
10 11	of the locomotor system. [Portuguese]. Acta medica portuguesa 1991;4(6):293-96.
12	12. Foley J, Vasily DB, Bradle J, et al. 830 nm light-emitting diode (led) phototherapy significantly reduced
13	return-to-play in injured university athletes: a pilot study. <i>Laser therapy</i> 2016;25(1):35-42. doi:
14	10.5978/islsm.16-OR-03 [published Online First: 2016/05/04]
15	13. Jastifer JR, Catena F, Doty JF, et al. Low-Level Laser Therapy for the Treatment of Chronic Plantar
16	Fasciitis: A Prospective Study. <i>Foot & ankle international</i> 2014;35(6):566-71. doi:
17	10.1177/1071100714523275 [published Online First: 2014/02/11]
18	14. Lögdberg-Andersson M MS, Hazel Å Low level laser therapy of tendinitis and myofascial pain. A
19 20	randomised double-blind controlled study. <i>Laser Therapy</i> 1997;9:79-86.
20 21	15. Mardh A, Lund I. High Power Laser for Treatment of Achilles Tendinosis - a Single Blind Randomized
22	Placebo Controlled Clinical Study. <i>Journal of lasers in medical sciences</i> 2016;7(2):92-8. doi:
23	10.15171/jlms.2016.16 [published Online First: 2016/06/23]
24	· · ·
25	16. Meier JK, K Traitement laser de la tendinite. <i>Médecine et hygiène</i> 1988;46(1741):907-11.
26	17. Morimoto Y, Saito A, Tokuhashi Y. Low level laser therapy for sports injuries. <i>Laser therapy</i>
27	2013;22(1):17-20. [published Online First: 2013/10/25]
28 29	18. Mulcahy D, McCormack D, McElwain J, et al. Low level laser therapy: a prospective double blind trial
29 30	of its use in an orthopaedic population. <i>Injury</i> 1995;26(5):315-17. doi: <u>https://doi.org/10.1016/0020-1383(95)00048-E</u>
31	19. Notarnicola A, Maccagnano G, Tafuri S, et al. CHELT therapy in the treatment of chronic insertional
32	Achilles tendinopathy. Lasers Med Sci 2014;29(3):1217-25. doi: 10.1007/s10103-013-1510-3
33	[published Online First: 2013/12/20]
34	20. Oliveira FS, Pinfildi CE, Parizoto NA, et al. Effect of low level laser therapy (830 nm) with different
35 36	therapy regimes on the process of tissue repair in partial lesion calcaneous tendon. <i>Lasers in surgery</i>
30 37	and medicine 2009;41(4):271-76. doi: http://dx.doi.org/10.1002/lsm.20760
38	
39	21. Orellana Molina A, Hernandez Diaz A, Larrea Cox PJ, et al. Laser infrarrojo frente a acupuntura en el
40	tratamiento del espolon calcaneo (Infrared laser versus acupuncture in the treatment of heel spurs)
41	[Spanish]. Revista de la Sociedad Espanola del Dolor 2010 Mar; 17(2):69-77 2010
42	22. Saxena A, St Louis M, Fournier M. Vibration and pressure wave therapy for calf strains: a proposed
43	treatment. <i>Muscles Ligaments Tendons J</i> 2013;3(2):60-2. doi: 10.11138/mltj/2013.3.2.060 [published
44 45	Online First: 2013/07/28]
45 46	23. Scott A, Backman LJ, Speed C. Tendinopathy: Update on Pathophysiology. <i>Journal of Orthopaedic &</i>
40 47	Sports Physical Therapy 2015;45(11):833-41. doi: 10.2519/jospt.2015.5884
48	24. Siebert W, Seichert N, Siebert B, et al. What is the efficacy of "soft" and "mid" lasers in therapy of
49	tendinopathies? A double-blind study. Archives of Orthopaedic and Trauma Surgery 1987
50	Oct;106(6):358-363 1987
51	25. Simunovic Z. Low level laser therapy with trigger points technique: A clinical study on 243 patients.
52	Journal of Clinical Laser Medicine and Surgery 1996;14(4):163-67.
53	26. Suleymanoglu T, Esmaeilzadeh S, Sen EI, et al. The effects of radial shock wave therapy and low level
54 55	laser therapy in the treatment of chronic plantar fasciitis: A randomized controlled trial. Annals of the
56	Rheumatic Diseases Conference: Annual European Congress of Rheumatology of the European
57	League Against Rheumatism, EULAR 2014;73(no pagination) doi:
58	http://dx.doi.org/10.1136/annrheumdis-2014-eular.3359
59	
60	

- 27. Takla MKN, Rezk SSR. Clinical effectiveness of multi-wavelength photobiomodulation therapy as an adjunct to extracorporeal shock wave therapy in the management of plantar fasciitis: a randomized controlled trial. *Lasers in Medical Science 2019 Apr;34(3):583-593* 2019
- 28. Tumilty S, Baxter GD. Heavy load eccentric exercise for achilles tendinopathy; too much of a good thing? *Physiotherapy (United Kingdom)* 2015;101:eS1546-eS47. doi: http://dx.doi.org/org/10.1016/j.physio.2015.03.1541

29. Tumilty S, Mani R, Baxter GD. Photobiomodulation and eccentric exercise for Achilles tendinopathy: a randomized controlled trial. *Lasers in Medical Science 2016 Jan;31(1):127-135* 2016

to per terien on

Page	39	of	39

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Page 1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	Page 1
INTRODUCTIO	DN		
Rationale	3	Describe the rationale for the review in the context of what is already known.	Page 2-3
		Page 3	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Page 1
Eligibility criteria6Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.		Page 3	
sources coverage, contact with stu		Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Page 3
		Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary material
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Page 3
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Page 3-4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Page 3-4
Risk of bias in individual12Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.		Page 3	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Page 4
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I ²) for each meta-analysis.	Page 4

1
2
3
4
5
6
7
/
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
21
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
47 48
49
50
51
52
53
54
55
56
57
58
59
60

PRISMA	checklist ((continued)	
i itionin i	encennor (continuea)	

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Page 3 and 10
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Page 9-10 + supplementary material
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Page 4 + figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1-2 and figure 2- 8
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Page 10-11 and table 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	figure 2-8
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Page 7-10 and figure 2- 8 + supplementary material
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Page 10
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Page 10 and supplementary material
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Page 11-13
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Page 13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Page 13
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	Page 14

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Efficacy of low-level laser therapy in patients with lower extremity tendinopathy or plantar fasciitis: systematic review and meta-analysis of randomised controlled trials

Journal:	BMJ Open
Manuscript ID	bmjopen-2021-059479.R1
Article Type:	Original research
Date Submitted by the Author:	16-Aug-2022
Complete List of Authors:	Naterstad, Ingvill; Universitetet i Bergen, Department of Global Public Health and Primary Care Joensen, Jon; Universitetet i Bergen, Department of Global Public Health and Primary Care Bjordal, Jan; Universitetet i Bergen, Department of Global Public Health and Primary Care Couppe, C; Bispebjerg Hospital, Institute of Sports Medicine Copenhagen Lopes-Martins, Rodrigo; UniEVANGELICA University Centre of Anapolis, Post Graduate Program in Human Movement and Rehabilitation (PPGMHR) Stausholm, Martin; University of Bergen, Department of Global Public Health and Primary Care
Primary Subject Heading :	Sports and exercise medicine
Secondary Subject Heading:	Rehabilitation medicine, Pathology
Keywords:	Laser therapy < DERMATOLOGY, GENERAL MEDICINE (see Internal Medicine), REHABILITATION MEDICINE

SCHOLARONE[™] Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

terez oni

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Page 2 of 38

2		
3		
4	1	Efficacy of low-level laser therapy in patients with lower extremity
5 6		
7	2	tendinopathy or plantar fasciitis: systematic review and meta-analysis
8	3	of randomised controlled trials
9	4	Ingvill Fjell Naterstad ¹ , Jon Joensen ¹ , Jan Magnus Bjordal ¹ , Christian Couppé ^{2,3} , Rodrigo Alvaro
10	5	Brandão Lopes-Martins ⁴ , Martin Bjørn Stausholm ¹
11	6	¹ Department of Global Public Health and Primary Care, University of Bergen, Bergen, Norway
12	7	² Institute of Sports Medicine Copenhagen, Bispebjerg Hospital, Copenhagen, Denmark
13 14	8	³ Center for Healthy Aging, Faculty of Health and Medical Sciences, University of Copenhagen,
15	9	Copenhagen, Denmark
16	10	⁴ Post Graduate Program in Human Movement and Rehabilitation, Universidade Evangélica de
17	11	Goiás, Anápolis, Brazil
18	12	
19	13	Correspondence to: Ingvill Fjell Naterstad naterstad@gmail.comWord count: 4774
20 21		
21	14	Abstract
23	15	Objectives We investigated the effectiveness of low-level laser therapy (LLLT) in lower extremity
24	16	tendinopathy and plantar fasciitis on patient-reported pain and disability.
25	17	Design Systematic review and meta-analysis.
26	18	Data sources Eligible articles in any language were identified through PubMed, Embase and
27	19	Physiotherapy Evidence Database (PEDro) on the 20th August 2020, references, citations and
28 29	20	experts.
30	21	Eligibility criteria for selection of studies Only randomised controlled trials involving participants
31	22	with lower extremity tendinopathy or plantar fasciitis treated with LLLT were included.
32	23	Data extraction and synthesis Random effects meta-analyses with dose subgroups based on the
33	24	World Association for Laser Therapy (WALT) recommendations were conducted. Risk-of-bias was
34	25	assessed with the PEDro scale.
35	26	Results LLLT was compared with placebo (10 trials), other interventions (5 trials) and as an add-on
36 37	27	intervention (3 trials). The study quality was moderate to high.
38	28	Overall, pain was significantly reduced by LLLT at completed therapy (13.15 mm Visual Analogue
39	29	Scale (VAS; 95% CI: 7.83-18.48)) and 4-12 weeks later (12.56 mm VAS (95% CI: 5.69-19.42)).
40	30	Overall, disability was significantly reduced by LLLT at completed therapy (Standardised Mean
41	31	Difference (SMD) = $0.39 (95\% \text{ CI: } 0.09-0.7)$ and 4-9 weeks later (SMD = $0.32 (95\% \text{ CI: } 0.05-0.7)$)
42	32	0.59)). Compared with placebo-control, the recommended doses significantly reduced pain at
43 44	33	completed therapy (14.98 VAS mm (95% CI: 3.74-26.22)) and 4-8 weeks later (14.00 mm VAS
45	34	(95% CI: 2.81-25.19)). The recommended doses significantly reduced pain as an add-on to exercise
46	35	therapy versus exercise therapy alone at completed therapy (18.15 mm VAS (95% CI: 10.55-
47	36	25.76)) and 4-9 weeks later (15.90 mm VAS (95% CI: 2.3-29.51)). No adverse events were
48	37	reported.
49	38	Conclusion LLLT significantly reduces pain and disability in lower extremity tendinopathy and
50 51	39	plantar fasciitis in the short and medium term. Long-term data was not available. Some uncertainty
51 52	40	about the effect size remains due to wide confidence intervals and lack of large trials.
53	41	PROSPERO registration number CRD42017077511
54	42	Keywords Phototherapy; Laser therapy; Tendinopathy; Plantar Fasciitis; Systematic review; Meta-
55	43	analysis
56		
57		
58		

Strengths and limitations of this study

- This review was performed in conformance with a prospective published protocol, which included a plan for subgrouping the trials by laser dose.
- There were no language restrictions; two (11%) of the included trials were reported in non-English language.
- The review includes results from an unpublished trial.
- ► The review features meta-analyses with direct comparisons between low-level laser therapy and placebo, other interventions, and no intervention.
- Only one reviewer extracted the data from the included trials, but the extracted data were checked for correctness by another reviewer.

INTRODUCTION

Tendinopathy and plantar fasciitis are disorders associated with substantial pain and loss of function in the lower extremity, especially prevalent in the athletic population but also common in the non-athletic population[1-3]. The aetiology of tendinopathy and plantar fasciitis is multifactorial and not fully understood. Risk factors for tendinopathy include overuse, acute trauma, ageing and genetic predisposition[4, 5]. Known risk factors for plantar fasciitis are prolonged standing and jumping, reduced ankle dorsiflexion and obesity[6-9]. Disorganised and degenerating collagen fibres, increased numbers of fibroblasts, altered composition of extracellular matrix proteins, formation of new vessels and rounding of tendon cells can be found in both tendinopathy and plantar fasciitis [10, 11].

Conservative treatment for lower extremity tendinopathy and plantar fasciitis includes an array of modalities and approaches. The effect of exercise therapy in tendinopathy is well-established, and any exercise type is preferential to wait-and-see in the earlier stages of tendinopathy [12]. However, a superiority of exercise therapy compared with other interventions has not been demonstrated. The use of non-steroidal anti-inflammatory drugs (NSAIDs) are frequently recommended in the early stages of tendinopathy and plantar fasciitis [13-15], even though the effectiveness of these drugs in lower extremity tendinopathies has only been investigated in a few placebo-controlled trials [16-20]. Moreover, NSAIDs have well known potentially fatal side-effects, most importantly severe cardiovascular events and gastrointestinal toxicity [21]. Low-level laser therapy (LLLT), also known as photobiomodulation therapy, is a quickly administered non-invasive intervention option free from negative side-effects. LLLT is an athermic photochemical modality, where red or near-infrared light is used to stimulate tissue healing and reduce pain and inflammation [22-25]. The working mechanisms of LLLT are partly established. There is evidence that LLLT increases adenosine triphosphate production [26], modulates the reactive oxygen species and the induction of transcription factors [27-30]. Furthermore, it has been demonstrated that LLLT inhibits cyclooxygenase-2 gene expression and prostaglandin E_2 (PGE₂) production in tendons[31, 32] and inhibits matrix metalloproteinase activity[32, 33]. In addition, under application of LLLT, macrophages are more likely to act as phagocytes[34].

There are heterogeneous results from clinical trials of LLLT on tendinopathies, and this may or may not be explained by a dose-response relationship[35-37]. Variation in LLLT parameters, such as wavelength, power density, pulse structure, application method and time-point of assessment may affect the treatment outcome. The World Association for Laser Therapy (WALT) has published treatment recommendations regarding the minimum LLLT doses required to reach a positive result[38, 39]. In a review by our research group regarding the effectiveness of LLLT in knee osteoarthritis, a significant dose-response relationship was discovered when the included trials were subgrouped using the WALT treatment recommendations for minimum dosage[40].

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

3 4 Furthermore, in a more recent placebo-controlled trial, we found some evidence that an upper limit 82 5 for the effectiveness of LLLT exists in knee osteoarthritis[41]. These clinical observations are in 83 6 line with the results of several in vivo and in vitro trials [42-45]. Whether such biphasic dose-84 7 response relationship exists in tendon disorders is unclear. Prior systematic reviews have 85 8 investigated LLLT in Achilles tendinopathy or plantar fasciitis[12, 46-51]. Unfortunately, these 9 86 10 reviews have one or more substantial limitations, such as a lack of a dose-response analysis[12], a 87 11 lack of inclusion of trials reported in non-English languages[46-50], or the faulty use of a fixed 88 12 effects meta-analysis model in the presence of highly heterogeneous studies[51]. Thus, the evidence 89 13 90 regarding the effectiveness of LLLT on pain and disability in lower limb tendinopathy and plantar 14 fasciitis is still somewhat unclear. Therefore, the objectives of the current review were to estimate 91 15 the effectiveness of LLLT in tendinopathy and plantar fasciitis on patient-reported pain and 92 16 disability using a dose-response analysis. 17 93

¹⁹ 94 **METHODS**

1 2

18

This review was conducted in adherence to a prospectively registered PROSPERO protocol and is reported in accordance with the Preferred Reporting Items of Systematic reviews and Meta-

²² 96 reported in accordance with th ²³ 97 Analysis statement 2009[52].

2425 98 Literature search and selection of studies

We included randomised clinical trials in which the effectiveness of LLLT in tendon disorders of
 the lower extremity or plantar fasciitis was compared with sham (placebo) LLLT, other
 interventions or no intervention, in terms of self-reported pain and/or disability. There were no
 restrictions regarding publication date and language.

A search for eligible reports of trials were conducted in the databases PubMed, Embase and Physiotherapy Evidence Database (PEDro) on the 20th August 2020. Furthermore, references from relevant systematic reviews[47, 49, 51, 53, 54] and all the included trials were screened, and experts in the field were asked to provide additional published and unpublished trials. Abstracts were not included. The PubMed search string is included in the supplementary material.

36 108 Two independent reviewers (IFN and MBS) read the titles/abstracts of the publications 37 109 identified by the search. Any article judged potentially eligible by a reviewer was retrieved in full 38 text. The same two reviewers evaluated the full texts of all the potentially eligible articles and made 110 39 a careful decision to include or exclude each article, with close attention to the eligibility criteria. 111 40 41 112 Any article not fulfilling the eligibility criteria was excluded and had its details listed with reason 42 113 for exclusion (supplementary material). Selection disagreements were resolved by discussion to 43 114 consensus with the option of a third person's (JJ) final decision if necessary. 44

45 115 **Risk-of-bias analysis**

Two reviewers (IFN and MBS) independently assessed the risk-of-bias of the included trials with the 0-10 points PEDro scale[55]. This was done on outcome level, and since the outcomes of

- the 0-10 points PEDro scale[55]. This was done on outcome level, and since the outcomes of
- interest were patient-assessed pain and disability, the participants were considered the assessors.
 Therefore, the assessors can only be blinded in placebo-controlled trials. When risk-of-bias
- Therefore, the assessors can only be blinded in placebo-controlled trials. When risk-of-bias
 disagreements could not be resolved by discussion, a third reviewer (JJ) made the final consensus-
- based decision. The trials were labelled as being of 'high', 'moderate' or 'poor' methodological quality if they had a total PEDro score of \geq 7, 5-6 or \leq 4, respectively[56]. Risk of small study bias was assessed with a funnel plot and by comparing the difference between the point effect estimates
- ⁵⁵ 123 was assessed with a fumier plot and by compa⁵⁶ 124 from random and fixed effects meta-analyses.
- 57 58 125 **Data-extraction and meta-analysis**
- 59 60

BMJ Open

- 4 Extraction of the following information was mandatory: number of participants allocated to laser 126 5 and control groups, participant characteristics, type and duration of interventions, laser-specific 127 6 application information (location of application, wavelength, energy density per treated spot, 128 7 number of spots treated, mean power density per treated spot, treatment time per spot, treated area, 129 8 9 laser sessions per week and total number of laser sessions, selected outcome measurement scales for 130 10 131 data-extraction, time-points of assessments, effect estimates and adverse events. 11
- The data collection was handled in a two-person procedure by IFN and MBS. One reviewer entered all the data in Excel sheets and the data were subsequently checked for correctness by another reviewer. If data-extraction disagreements could not be resolved by discussion, a third reviewer (JMB) made the final consensus-based decision.
- All the meta-analyses were conducted using random effects models, weighting the individual trial results relatively even when statistical heterogeneity is present[57].
- 18 The pain results were synthesised using the Mean Difference (MD) method as this method 138 19 139 allows for change and final scores to be combined [58]. Pain scores reported on the Visual Analogue 20 Scale (VAS) and on the Numeric Rating Scale highly correlates[59] and were thus considered the 140 21 same. Self-reported disability results were synthesised with the Standardised Mean Difference 141 22 (SMD) method using change scores solely [58]. According to Cohen, a SMD of 0.2, 0.5 and 0.8 can 142 23 be considered small, moderate and large, respectively [58]. 24 143
- 25 144 Heterogeneity was measured using I²-statistics (inconsistency)[60]. An inconsistency level 26 145 of 25%, 50% and 75% would be considered low, moderate and high, respectively[61]. Standard 27 146 deviations (SD) for meta-analysis were extracted or estimated from other variance data in the 28 following prioritised order: SD, standard error, 95 % confidence interval, p-value, interquartile 147 29 range, median of correlations, visually from graph, correlation of 0.6 or mean of SDs from similar 148 30 31 149 trials.
- Trials were subgrouped by laser dose using the WALT treatment recommendations[62, 63], 32 150 33 151 as specified in the a priori protocol. WALT recommends irradiating minimum of 2-3 points on the 34 152 tendon or fascia. In Achilles and patellar tendinopathy, the recommended dose with 904 nm 35 wavelength laser is minimum 2 joules per point. When utilizing 780-860 nm wavelength laser, the 153 36 minimum dose is 4 Joules per point. In plantar fasciitis, the recommended minimum dose is 2 joules 154 37 per point with a 904 nm wavelength laser or 4 joules per point with 780-860 nm wavelength laser. 155 38 We subgrouped the trials as recommended dose and non-recommended laser dose. If the trial 39 156 reports lacked sufficient dose parameters to be identified as recommended or non-recommended 40 157 41 158 dose, they were categorised as unclear laser dose.
- Two time-points of assessment were selected for analysis, that is, immediately after the end of LLLT and last time-point of assessment 2-14 weeks after completed LLLT (follow-up).
- IFN and MBS performed the meta-analyses, using Excel 2016 (Microsoft) and Review
 Manager Version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration,
 2014).

49 164 **Patient and public involvement**

⁵⁰ 165 Patients or the public were not involved in the conceptualization or carrying out of this research.

⁵² 166 **RESULTS**

A total of 870 records were identified in the search, of which 18 reports of trials (n = 784) were included in review and meta-analysis (Figure 1 and Table 1). LLLT was applied to participants with patellar tendinopathy in two trials, Achilles tendinopathy in five trials and plantar fasciitis in 11 trials. LLLT was compared with placebo in 10 trials, other interventions in five trials and as an adjunct intervention in three trials. Two trials were reported in non-English language, and one trial

60

was unpublished (Naterstad et al.). The excluded articles were listed with reasons for omission
(supplementary material). The mean age of the participants was 43.6 (minimum <18, maximum
54.5, data from 14 trials), and the mean baseline pain intensity was 64.2 mm on the VAS (minimum
19.3 mm, maximum 85 mm, data from 18 trials). No adverse events were reported by any of the
trial authors. None of the trial authors declared that they had received funding from the laser
industry.

First author, year	Participants at baseline (intervention)*	Participants at baseline (control)*	Intervention versus control	Outcome and time of reassessment after baseline (time used for analysis in bold
Patellar tendinopat	hy			
Liu 2014 [64] , LLLT versus ET	n: 7 Age years: ≥ 18 , ≤ 23 VAS pain mm:	n: 7 Age years: $\geq 18, \leq$ 23 VAS pain mm:	4 weeks of LLLT versus 4 weeks of eccentric ET	Pain: VAS Disability: Modified-VISA Reassessment: 4 weeks
	67.9±13.2	65.7±15.4		
Liu 2014 [64] , LLLT+ET versus ET	n: 7 Age years: ≥ 18 , ≤ 23 VAS pain mm:	n: 7 Age years: $\geq 18, \leq 23$ VAS pain mm:	4 weeks of LLLT and eccentric exercise therapy versus 4 weeks of eccentric ET	Pain: VAS Disability: Modified-VISA Reassessment: 4 weeks
	67.9±12.2	65.71±15.4		
Stergioulas 2003 [65]	n: 23 Age years: 29.2±13.4 VAS pain mm: 81.7±13.4	n: 21 Age years: 29.8±13.8 VAS pain mm: 75.9±18.8	2 weeks of LLLT versus 2 weeks of sham LLLT	Pain: VAS Disability: Functional Index Questionnaire Reassessment: 2 and 6 weeks
Achilles tendinopat				
Darre 1994 [66]	n: 46 Age years: ≥ 18 VAS pain mm: 58.5±37.9	n: 43 Age years: \geq 18 VAS pain mm: 72 \pm 34.3	2.4 weeks of LLLT versus 2.4 weeks of sham LLLT	Pain: VAS Disability: - Reassessment: 2.4 weeks
Naterstad**	n: 20 Age years: 45.4±14.7 VAS pain mm: 52.9±26.1	n: 21 Age years: 45.8±13.9 VAS pain mm: 53.8±26.7	4 weeks of LLLT and cryotherapy and 12 weeks of eccentric and concentric ET versus 4 weeks of sham LLLT and cryotherapy and 2 weeks of eccentric and concentric ET	Pain: THIP VAS most painful activity Disability: THIP VAS ADL Reassessment: 4 and 12 weeks
Stergioulas 2008 [67]	n: 20 Age years: 30.1±4.8 VAS pain mm: 79.8±9.5	n: 20 Age years: 28.8±4.8 VAS pain mm: 81.8±11.6	8 weeks of LLLT and eccentric ET versus 8 weeks of sham LLLT and eccentric ET	Pain: VAS during activity Disability: - Reassessment: 4, 8 and 12 weeks
Tumilty 2008 [68]	n: 10 Age years: 41.4±7.6 VAS pain mm: 47.8±25.9	n: 10 Age years: 42.5±8.5 VAS pain mm: 39±20.2	4 weeks of LLLT and 12 weeks of eccentric ET versus 4 weeks of sham LLLT and 12 weeks of eccentric ET	Pain: VAS in morning Disability: - Reassessment: 4 and 12 weeks
Tumilty 2012 [69]	n: 20 Age years: 45.6±9.1 NRS pain mm: 21.1±1.17	n: 20 Age years: 46.5±6.4 NRS pain mm: 19.3±0.94	4 weeks of LLLT and 12 weeks of eccentric ET versus 4 weeks of sham LLLT and 12 weeks of eccentric ET	Pain: NRS Disability: - Reassessment: 4 , 12 and 52 weeks
Plantar fasciitis				
Basford 1998 [70]	n: 16 Age years: 42.5 (26-64)* VAS pain mm: 57.9 (22.2-97)*	n: 15 Age years: 42 (33- 51)* VAS pain mm: 46.6 (4-86)* (4 weeks of LLLT versus 4 weeks of sham LLLT	Pain: Pain when walking in morning Disability: Limping in morning Reassessment: 2, 4 and 8 weeks

С	5 Sinar 2017[71]	n: 29	n: 22	3 weeks of LLLT and stretching versus 3	Pain: VAS
		Age years:	Age years:	weeks of stretching	Disability: AOFAS-F activity
		46.59±10.1	44.18±9.7		limitations
		VAS pain mm:	VAS pain mm:		Reassessment: 3 and 12 week
C	inar 2018 [72]	61.3±19.4 n: 24	54.9±19.7 n: 17	3 weeks of LLLT and 12 weeks of	Pain: NRS
C	linai 2018[7 2]	Age years:	Age years: 44±8.6	stretching versus 12 weeks of stretching	Disability: -
		46.5±10.3	NRS pain mm:	Stetening versus 12 weeks of stetening	Reassessment: 3 and 12 weel
		NRS pain mm:	6.2±2.14		
		6.3±1.42			
	inar 2018 [72] ,	n: 24	n: 25	3 weeks of LLLT and 12 weeks of	Pain: NRS
E	SWT	Age years:	Age years:	stretching versus 3 weeks of ESWT (2000	Disability: - Reassessment: 3 and 12 week
		46.5±10.3	45.4±9.7	mJ/mm ² , session once per week) and 12	Reassessment. 5 and 12 week
		NRS pain mm: 6.3±1.42	NRS pain mm: 6.7±2.67	weeks of stretching	
E	lsehrawy	n: 23	n:23	3 weeks of LLLT versus 2 weeks of ESWT	Pain: VAS
	018 [73]	Age years:	Age years: 46±10.2	(2050 shocks/min, 10 Hz, 2.5 bars once per	Disability: FFI disability
	L - J	46.4±10	VAS pain: 82±15	week)	subscale
		VAS pain: 85±8	-	·	Reassessment: 4 weeks
K	liritsi 2010 [74]	n: 15	n: 15	6 weeks of LLLT versus 6 weeks of sham	Pain: ADL VAS
		Age years:	Age years: 41±12	LLLT	Disability: -
		41±12	VAS pain mm:		Reassessment: 6 weeks
		VAS pain mm: 67±8.3	67±9.3		
ĸ	loteeswaran	67±8.3 n: 15	n: 15	2 weeks of LLLT and stretching versus 2	Pain: NRS
	020 [75]	Age years: 30-	Age years: 30-60	weeks of TUS and stretching	Disability: FAAM
2.	· · [. •]	60	NRS pain: 72.7±8		Reassessment: 2 weeks
		NRS pain:	1		
		74.7±11.9			
L	amba 2013 [76]	n: 40	n: 40	4 weeks of LLLT and stretching versus 4	Pain: VAS
		Age years:	Age years:	weeks of sham LLLT and stretching	Disability: -
		40.9±10.4 VAS pain mm:	40.4±9.7 VAS pain mm:		Reassessment: 1,2, 3 and 4 weeks
		57.5±10.8	62±7.6		WEEKS
Ν	facias 2015[77]	n: 37	n: 32	3 weeks of LLLT versus 3 weeks of sham	Pain: VAS heel pain
		Age years: ≥ 18	Age years: ≥ 18	LLLT	Disability: FFI disability
		VAS pain mm:	VAS pain mm:		subscale 8 weeks
		69.1±12.7	67.6±11.8		Reassessment: 1, 2, 3, 6 and
~	1 00107-01	17	17	4 1 6777 2	weeks
S	anmak 2019 [78]	n: 17	n: 17	4 weeks of LLLT versus 3 weeks of ESWT (2 bar with 2,000 shocks/min at 10 Hz once	Pain: VAS
		Age years: 53* VAS pain mm:	Age years: 49* VAS pain mm: 80*	(2 bar with 2,000 shocks/min at 10 Hz once per week)	Reassessment: 4 and 8 weeks
		70*	• AS pain min. 60*	- /	
U	lusoy 2017 [79] ,	n: 20	n: 20	3 weeks of LLLT versus 3 weeks of TUS (1	Pain: VAS in morning
	US	Age years: 53.4	Age years: 50.95	mHz; 2 W/cm2)	Disability: -
		VAS pain mm:	VAS pain mm:		Reassessment: 7 weeks
_		68.7	66.6		
	lusoy 2017 [79] ,	n: 20	n: 20	3 weeks of LLLT versus 3 weeks of ESWT	Pain: VAS in morning
E	SWT	Age years: 53.4±14.7	Age years: 54.4±6.9	(2.5 bar with 2,000 shocks/min at 10 Hz three times per week)	Disability: - Reassessment: 7 weeks
		VAS pain mm:	VAS pain mm:	unce unies per week)	Reassessment. / weeks
		68.7±12.5	66±11.2		
Y	üzer 2006[80]	n: 24	n: 30	1.4 weeks of LLLT versus steroid injection	Pain: VAS
		Age years:	Age years:	·	Disability: -
		49.6±1.2	51.5±11.5		Reassessment: 5.4, 13.4 and
		VAS pain mm:	VAS pain mm:		25.4 weeks
		80±12	76±15	otherwise indicated. *Median with or without i	

56 randomised controlled trial 181

ADL, activity of daily living; AOFAS-F, American Orthopedic Foot and Ankle Score Function; ESWT, Extracorporeal Shockwave Therapy; ET, 57 58

exercise therapy; FAAM, Foot and ankle ability measurement questionnaire; FFI, Foot Function Index; LLLT, Low-Level Laser Therapy; NRS, Numeric Rating Scale; THIP, Tendinopathy Health Impact Profile; TUS, therapeutic ultrasound; VAS, Visual Analogue Scale.

182 183 184

LLLT was compared with placebo LLLT in 10 trials [65, 66, 68-70, 74, 76, 77, 81], and exercise therapy or stretching exercises was applied as a co-intervention in five of these trials. LLLT was compared with exercise therapy or stretching exercises in three trials[64, 71, 72]. A comparison between LLLT and Extracorporeal Shockwave Therapy (ESWT) in plantar fasciitis was performed in four trials[72, 73, 78, 79]. LLLT was compared to therapeutic ultrasound in two trials[75, 79], and LLLT was compared to steroid injection in one trial[80]. Recommended laser doses were applied in at least 11 trials[64-68, 71, 72, 74, 76, 79] and a non-recommended dose was used in at least one trial[69]. We were unable to categorise the laser doses in the remaining six trials[70, 73, 75, 77, 78, 80] due to inadequately or missing descriptions of laser parameters (Table 2). Two different LLLT doses were applied in the same session in two of the trials [64, 74].

First author, year	Wave- length (nm)	Mean output power (mW)	Seconds per treatment spot (s)	Joules per treatment spot (J)	Number of spots treated	Number of sessions/Weeks	Dose recommended by WALT
Patellar tendinopathy							
Liu 2014[64]	810	200	600	-	$1 \times$	24/4	Yes
	810	200	300	-	2		
Stergioulas 2003[65]	904	50	300	1.2	10	10/2	Yes
Achilles tendinopathy							
Darre 1994[66]	830	30		4	4	12/2.5	Yes
Naterstad**	904	60	50	3	6	12/4	Yes
Stergioulas 2008[67]	820	30	-	0.9	6	12/8	Yes
Tumilty 2008[68]	810	100	30	3	6	12/4	Yes
Tumilty 2012[69]	810	7	30	0.21	6	12/4	No
Plantar fasciitis							
Basford 1998[70]	830	30	-	-	3 *	12/4	Unclear
Cinar 2017[71]	830	100	80	5.6	5	10/3	Yes
Cinar 2018[72]	830	100	80	5.6	5	10/3	Yes
Elsehrawy 2018[73]	830	-	-	-	3 *	6/3	Unclear
Kiritsi 2010[74]	904	60	-	8.4	$1 \times$	18/6	Yes
	904	60	-	-	2 *		
Koteeswaran 2020[75]	830	-	180	- 6	3	9/3	Unclear
Lamba 2013[76]	820	100	80	- /	3 *	12/4	Yes
Macias 2015[77]	635	17	600	-	3	6/3	Unclear
Sanmak 2019[78]	685	30	60	-	2 *	12/4	Unclear
Ulusoy 2017[79]	830	50	200	-	3*	15/3	Yes
Yüzer 2006[80]	904	-	30	-	-	10/1.4	Unclear

× Two different dosages applied within the same session.

*One or more spots/areas treated with movement of the laser probe.

**Naterstad et al. Efficacy of Low-level Laser Therapy as an addition to exercise and cryotherapy in chronic Achilles tendinopathy: a double-blinded randomised controlled trial

LLLT, Low-Level Laser Therapy; WALT, World Association for Laser Therapy.

Overall pain and disability results pain and disability - LLLT versus any control

Data allowing for a meta-analysis of an immediate pain change were available from 16 trials with recommended, non-recommended or unknown laser dosing.

Overall, pain was significantly reduced by LLLT over any control immediately after completed therapy (13.15 mm VAS (95% CI: 7.82 to 18.48), $I^2 = 65\%$, n = 784) (Figure 2) and at 52 206 follow-ups 4-12 weeks later (12.56 mm VAS (95% CI: 5.69 to 19.42), $I^2 = 48\%$, n = 556) (Figure 3).

Overall, the disability results immediately after completed therapy significantly favoured LLLT over any control (SMD = 0.39 (95% CI: 0.09 to 0.7), $I^2 = 30\%$, n = 260) (Figure 4). A disability reduction by LLLT remained significant at follow-ups 4-9 weeks after completed therapy $(SMD = 0.32 (95\% \text{ CI: } 0.05 \text{ to } 0.59), I^2 = 4\%, n = 222)$ (Figure 5). Overall and subgroup pain 58 211 results - LLLT versus placebo-control 59 212

BMJ Open

1	
2	
3	
4 213 5 213	Overall, pain was significantly reduced by LLLT over placebo-control immediately after completed
6 ²¹⁴	therapy (11.48 mm VAS (95% CI: 2.68 to 20.28), $I^2 = 73\%$, n = 507) (Figure 6) and during follow-
7 215	ups 4-8 weeks after completed therapy (13.62 mm VAS (95% CI: 2.18 to 25.06), $I^2 = 68\%$, $n = 277$)
8 216	(Figure 3).
9 217	The recommended laser doses significantly reduced pain compared with placebo
10 217	
	immediately after completed therapy (14.98 mm VAS (95% CI: 3.74 to 26.22), $I^2 = 67\%$, n = 367)
12^{219}	(Figure 6). A non-recommended laser dose from a single trial provided no significant pain reduction
13 220	immediately after completed therapy (-3.0 mm VAS (95% CI: -11.17 to 5.7), $n = 40$) (Figure 6).
14 221	Trials with unknown laser doses significantly favoured LLLT over placebo-control immediately
15 222	after completed therapy (10.83 mm VAS (95% CI: 2.44 to 19.21), $I^2 = 0\%$, n = 100). The between-
16 223	subgroup difference was significant ($p = 0.02$) (Figure 6).
17	
18 224	At follow-ups 4-8 weeks after completed therapy, the recommended laser doses significantly
19 ₂₂₅	reduced pain compared with placebo (14.00 mm VAS (95% CI: 2.81 to 25.19), $I^2 = 5\%$, n = 136)
²⁰ 226	(Figure S1, supplementary material). A non-recommended dose provided in a single trial did not
$\begin{array}{c} 21 \\ 22 \end{array} \begin{array}{c} 220 \\ 227 \end{array}$	significantly reduce pain compared with placebo at follow-up 8 weeks after completed therapy (0.0
22 23 ²²⁸	mm VAS (95% CI: -7.62 to 7.62), $n = 40$) (Figure S1, supplementary material). At follow-ups 4-5
23 229	weeks after completed therapy, trials with unknown laser doses demonstrated a significant pain
24 <i>229</i> 25 230	reduction by LLLT compared with placebo (23.94 mm VAS (95% CI: 14.39 to 33.48), $I^2 = 0\%$, n =
26 231	97) (Figure S1, supplementary material). The between-subgroup difference was significant (p <
27 ₂₃₂	0.001) (Figure S1, supplementary material). Subgroup pain results - LLLT versus no intervention
28 232	
28 233 29 234	Pain was significantly lowered by the recommended laser doses when used as an adjunct to
30 234	exercise, stretching and insoles over exercise, stretching and insoles alone, both immediately after
31 235	completed therapy (18.15 mm VAS (95% CI: 10.55 to 25.76), $I^2 = 0\%$, $n = 104$) (Figure S2,
32 236	supplementary material) and at follow-up 9 weeks after completed therapy (19.67 mm VAS (95%
33 237	CI: 5.16 to 34.18), $I^2 = 0\%$, $n = 80$) (Figure S3, supplementary material).
34 238	
35 239 36 240	Overall and subgroup pain results - LLLT versus other interventions
37 240	Overall, pain was significantly reduced by LLLT compared with other interventions immediately
38 ²⁴¹	after completed therapy (13.23 mm VAS (95% CI: 4.07 to 22.39), $I^2 = 66\%$, n = 173) (Figure S4,
39 242	supplementary material). Follow-up results of pain 4-12 weeks after completed therapy favoured
40 243	LLLT over other interventions, but not significantly (9.41 mm VAS (95% CI: -0.44 to 19.26), $I^2 =$
41 244	16%, n = 193) (Figure S5, supplementary material).
42 245	The recommended laser doses were compared with exercise therapy in one trial and ESWT
43 246	in another trial immediately after completed therapy and the pain results favoured LLLT, but not
44 247	significantly (13.91 mm VAS (95% CI: -1.34 to 29.15), $I^2 = 65\%$, n = 63) (Figure S4,
45 ²⁴⁷ 46 ²⁴⁸	supplementary material).
46 249	The pain results from three trials with unknown laser doses, in which two groups received
47 249 48 250	ESWT and one group received therapeutic ultrasound, favoured LLLT immediately after completed
49 251	therapy, but not significantly (12.88 mm VAS (95% CI: -1.29 to 27.04), $I^2 = 77\%$, n = 110) (Figure
50 ₂₅₂	S4, supplementary material).
51 253	At follow-ups 4-12 weeks after completed therapy, pain was significantly lowered by the
52 255	recommended laser doses compared with other interventions (15.90 mm VAS (95% CI: 2.30 to
53 ²⁵⁴	
54 ²⁵⁵	29.51), $I^2 = 0\%$, $n = 103$) (Figure S5, supplementary material). Pain was not significantly lowered
55 256	by unknown laser doses compared with other interventions at follow-ups 4-12 weeks after semilated thereas (2.02 mm VAS (050 / CL 15.8 to 21.(7) $12 = 520$ / $n = 87$) (Figure S5
56 257	completed therapy (2.93 mm VAS (95% CI: -15.8 to 21.67), $I^2 = 52\%$, n = 87) (Figure S5,
57 ₂₅₈ 58	supplementary material).
59	
60	

1

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

2		
3		
4	259	Overall and subgroup disability results - LLLT versus placebo-control
5 6	260	Overall, the disability results favoured LLLT over placebo-control immediately after completed
0 7	261	therapy, but not significantly (SMD = 0.2 (95% CI: -0.18 to 0.58), I ² = 0%, n = 107) (Figure 4). The
, 8	262	same applied to the follow-up results 4-8 weeks after completed therapy (SMD = 0.19 (95% CI: -
9	263	0.11 to 0.49), $I^2 = 0\%$, $n = 173$) (Figure S6, supplementary material).
10		The disability results immediately after completed therapy favoured the recommended laser
11	265	doses over other interventions, but not significantly (SMD = 0.25 (95% CI: -0.21 to 0.7), I ² = 0%, n
12	266	= 76) (Figure S7, supplementary material). The same applied to unknown laser doses compared
13 14	0.07	with placebo-control immediately after completed therapy (SMD = $0.10 (95\% \text{ CI: } -0.61 \text{ to } 0.8)$), n =
	268	31) (Figure S7, supplementary material).
	269	At follow-ups 4-8 weeks after completed therapy, the disability results favoured the
	270	recommended laser doses over other interventions, but not significantly (SMD = 0.24 (95% CI: -
	271	0.21 to 0.7), $I^2 = 0\%$, n = 76) (Figure S6, supplementary material). The same applied to the
19	272	unknown laser doses compared with placebo-control immediately after completed therapy (SMD =
20	273	0.14 (95% CI: -0.26 to 0.54), $I^2 = 0\%$, $n = 107$) (Figure S6, supplementary material).
21 22		
22	274	Overall and subgroup disability results - LLLT versus other interventions
	275	The overall disability results immediately after completed therapy favoured LLLT, but not
25	276	significantly (SMD = 0.58 (95% CI: -0.11 to 1.27), $I^2 = 56\%$, n = 90) (Figure 4).
	277	The recommended laser doses neither provided a significant disability reduction compared
27	278	with other interventions immediately after completed therapy (SMD = 0.2 (95% CI: -0.85 to 1.25),
28 29	279	n = 14) (Figure S8, supplementary material). The same applied to unknown laser doses compared
29 30	280	with other interventions immediately after completed therapy (SMD = 0.73 (95% CI: -0.26 to 1.72),
31	281	n = 76) (Figure S8, supplementary material).
32		
33	282	
		Subgroup disability results - LLLT versus no intervention
	283	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or
35	283 284	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68
35 36	283 284 285	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), I ² = 69%, n = 61) (Figure S9, supplementary material). At follow-up 9
35 36 37	283 284 285 286	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), $I^2 = 69\%$, n = 61) (Figure S9, supplementary material). At follow-up 9 weeks after completed therapy, disability was significantly lowered by the recommended laser
35 36 37 38 39	283 284 285 286 287	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), $I^2 = 69\%$, n = 61) (Figure S9, supplementary material). At follow-up 9 weeks after completed therapy, disability was significantly lowered by the recommended laser doses as an adjunct to stretching and insoles compared with exercise therapy and insoles alone
35 36 37 38 39	283 284 285 286	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), $I^2 = 69\%$, n = 61) (Figure S9, supplementary material). At follow-up 9 weeks after completed therapy, disability was significantly lowered by the recommended laser
35 36 37 38 39 40 41	283 284 285 286 287 288	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), $I^2 = 69\%$, n = 61) (Figure S9, supplementary material). At follow-up 9 weeks after completed therapy, disability was significantly lowered by the recommended laser doses as an adjunct to stretching and insoles compared with exercise therapy and insoles alone (SMD = 0.82 (95% CI: 0.24 to 1.41), n = 49) (Figure S10, supplementary material).
35 36 37 38 39 40 41 42	283 284 285 286 287 288 289	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), $I^2 = 69\%$, $n = 61$) (Figure S9, supplementary material). At follow-up 9 weeks after completed therapy, disability was significantly lowered by the recommended laser doses as an adjunct to stretching and insoles compared with exercise therapy and insoles alone (SMD = 0.82 (95% CI: 0.24 to 1.41), $n = 49$) (Figure S10, supplementary material).
35 36 37 38 39 40 41 42 43	283 284 285 286 287 288 289 290	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), $I^2 = 69\%$, n = 61) (Figure S9, supplementary material). At follow-up 9 weeks after completed therapy, disability was significantly lowered by the recommended laser doses as an adjunct to stretching and insoles compared with exercise therapy and insoles alone (SMD = 0.82 (95% CI: 0.24 to 1.41), n = 49) (Figure S10, supplementary material). <i>Sensitivity analysis of laser dose categorisation</i> The irradiation procedure by Darre et al.[66] was judged as a recommended laser dose, based on the
 35 36 37 38 39 40 41 42 43 44 	283 284 285 286 287 288 289 290 291	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), $I^2 = 69\%$, n = 61) (Figure S9, supplementary material). At follow-up 9 weeks after completed therapy, disability was significantly lowered by the recommended laser doses as an adjunct to stretching and insoles compared with exercise therapy and insoles alone (SMD = 0.82 (95% CI: 0.24 to 1.41), n = 49) (Figure S10, supplementary material). <i>Sensitivity analysis of laser dose categorisation</i> The irradiation procedure by Darre et al.[66] was judged as a recommended laser dose, based on the reported dose parameters in the paper. However, the dose description is somewhat sparse and could
35 36 37 38 39 40 41 42 43	283 284 285 286 287 288 289 290 291 292	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), $I^2 = 69\%$, $n = 61$) (Figure S9, supplementary material). At follow-up 9 weeks after completed therapy, disability was significantly lowered by the recommended laser doses as an adjunct to stretching and insoles compared with exercise therapy and insoles alone (SMD = 0.82 (95% CI: 0.24 to 1.41), $n = 49$) (Figure S10, supplementary material). <i>Sensitivity analysis of laser dose categorisation</i> The irradiation procedure by Darre et al.[66] was judged as a recommended laser dose, based on the reported dose parameters in the paper. However, the dose description is somewhat sparse and could be misinterpreted. If the study by Darre et al. was allocated to the unknown laser dose subgroup, the
35 36 37 38 39 40 41 42 43 44 45 46 47	283 284 285 286 287 288 289 290 291 292 293	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), $I^2 = 69\%$, $n = 61$) (Figure S9, supplementary material). At follow-up 9 weeks after completed therapy, disability was significantly lowered by the recommended laser doses as an adjunct to stretching and insoles compared with exercise therapy and insoles alone (SMD = 0.82 (95% CI: 0.24 to 1.41), $n = 49$) (Figure S10, supplementary material). <i>Sensitivity analysis of laser dose categorisation</i> The irradiation procedure by Darre et al.[66] was judged as a recommended laser dose, based on the reported dose parameters in the paper. However, the dose description is somewhat sparse and could be misinterpreted. If the study by Darre et al. was allocated to the unknown laser dose subgroup, the statistical heterogeneity would be eliminated in the recommended laser dose group and the
35 36 37 38 39 40 41 42 43 44 45 46 47 48	283 284 285 286 287 288 289 290 291 292 293 294	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), $I^2 = 69\%$, $n = 61$) (Figure S9, supplementary material). At follow-up 9 weeks after completed therapy, disability was significantly lowered by the recommended laser doses as an adjunct to stretching and insoles compared with exercise therapy and insoles alone (SMD = 0.82 (95% CI: 0.24 to 1.41), $n = 49$) (Figure S10, supplementary material). <i>Sensitivity analysis of laser dose categorisation</i> The irradiation procedure by Darre et al.[66] was judged as a recommended laser dose, based on the reported dose parameters in the paper. However, the dose description is somewhat sparse and could be misinterpreted. If the study by Darre et al. was allocated to the unknown laser dose subgroup, the statistical heterogeneity would be eliminated in the recommended laser dose group and the estimated pain reduction would be increased to 21.12 mm VAS ((95% CI: 14.94 to 27.31), $I^2 = 0\%$,
35 36 37 38 39 40 41 42 43 44 45 46 47 48 49	283 284 285 286 287 288 289 290 291 292 293	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), $I^2 = 69\%$, $n = 61$) (Figure S9, supplementary material). At follow-up 9 weeks after completed therapy, disability was significantly lowered by the recommended laser doses as an adjunct to stretching and insoles compared with exercise therapy and insoles alone (SMD = 0.82 (95% CI: 0.24 to 1.41), $n = 49$) (Figure S10, supplementary material). <i>Sensitivity analysis of laser dose categorisation</i> The irradiation procedure by Darre et al.[66] was judged as a recommended laser dose, based on the reported dose parameters in the paper. However, the dose description is somewhat sparse and could be misinterpreted. If the study by Darre et al. was allocated to the unknown laser dose subgroup, the statistical heterogeneity would be eliminated in the recommended laser dose group and the
35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50	283 284 285 286 287 288 289 290 291 292 293 294 295	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), $I^2 = 69\%$, $n = 61$) (Figure S9, supplementary material). At follow-up 9 weeks after completed therapy, disability was significantly lowered by the recommended laser doses as an adjunct to stretching and insoles compared with exercise therapy and insoles alone (SMD = 0.82 (95% CI: 0.24 to 1.41), $n = 49$) (Figure S10, supplementary material). <i>Sensitivity analysis of laser dose categorisation</i> The irradiation procedure by Darre et al.[66] was judged as a recommended laser dose, based on the reported dose parameters in the paper. However, the dose description is somewhat sparse and could be misinterpreted. If the study by Darre et al. was allocated to the unknown laser dose subgroup, the statistical heterogeneity would be eliminated in the recommended laser dose group and the estimated pain reduction would be increased to 21.12 mm VAS ((95% CI: 14.94 to 27.31), $I^2 = 0\%$, $n = 278$) versus placebo immediately after completed therapy (Figure S11, supplementary material).
35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51	283 284 285 286 287 288 289 290 291 292 293 294 295 296	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), $I^2 = 69\%$, $n = 61$) (Figure S9, supplementary material). At follow-up 9 weeks after completed therapy, disability was significantly lowered by the recommended laser doses as an adjunct to stretching and insoles compared with exercise therapy and insoles alone (SMD = 0.82 (95% CI: 0.24 to 1.41), $n = 49$) (Figure S10, supplementary material). <i>Sensitivity analysis of laser dose categorisation</i> The irradiation procedure by Darre et al.[66] was judged as a recommended laser dose, based on the reported dose parameters in the paper. However, the dose description is somewhat sparse and could be misinterpreted. If the study by Darre et al. was allocated to the unknown laser dose subgroup, the statistical heterogeneity would be eliminated in the recommended laser dose group and the estimated pain reduction would be increased to 21.12 mm VAS ((95% CI: 14.94 to 27.31), $I^2 = 0\%$, $n = 278$) versus placebo immediately after completed therapy (Figure S11, supplementary material). <i>Risk-of-bias within studies</i>
35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52	283 284 285 286 287 288 289 290 291 292 293 294 295 296 297	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), $I^2 = 69\%$, $n = 61$) (Figure S9, supplementary material). At follow-up 9 weeks after completed therapy, disability was significantly lowered by the recommended laser doses as an adjunct to stretching and insoles compared with exercise therapy and insoles alone (SMD = 0.82 (95% CI: 0.24 to 1.41), $n = 49$) (Figure S10, supplementary material). <i>Sensitivity analysis of laser dose categorisation</i> The irradiation procedure by Darre et al.[66] was judged as a recommended laser dose, based on the reported dose parameters in the paper. However, the dose description is somewhat sparse and could be misinterpreted. If the study by Darre et al. was allocated to the unknown laser dose subgroup, the statistical heterogeneity would be eliminated in the recommended laser dose group and the estimated pain reduction would be increased to 21.12 mm VAS ((95% CI: 14.94 to 27.31), $I^2 = 0\%$, $n = 278$) versus placebo immediately after completed therapy (Figure S11, supplementary material). <i>Risk-of-bias within studies</i> Ten of the included trials were found to be of high methodological quality, and the remaining eight
35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51	283 284 285 286 287 288 289 290 291 292 293 294 295 294 295 296 297 298	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), $I^2 = 69\%$, $n = 61$) (Figure S9, supplementary material). At follow-up 9 weeks after completed therapy, disability was significantly lowered by the recommended laser doses as an adjunct to stretching and insoles compared with exercise therapy and insoles alone (SMD = 0.82 (95% CI: 0.24 to 1.41), $n = 49$) (Figure S10, supplementary material). Sensitivity analysis of laser dose categorisation The irradiation procedure by Darre et al.[66] was judged as a recommended laser dose, based on the reported dose parameters in the paper. However, the dose description is somewhat sparse and could be misinterpreted. If the study by Darre et al. was allocated to the unknown laser dose subgroup, the statistical heterogeneity would be eliminated in the recommended laser dose group and the estimated pain reduction would be increased to 21.12 mm VAS ((95% CI: 14.94 to 27.31), $I^2 = 0\%$, $n = 278$) versus placebo immediately after completed therapy (Figure S11, supplementary material). <i>Risk-of-bias within studies</i> Ten of the included trials were found to be of high methodological quality, and the remaining eight included trials were found to be of moderate methodological quality. All the trials
35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55	283 284 285 286 287 288 289 290 291 292 293 294 295 296 297 298 299	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), $I^2 = 69\%$, $n = 61$) (Figure S9, supplementary material). At follow-up 9 weeks after completed therapy, disability was significantly lowered by the recommended laser doses as an adjunct to stretching and insoles compared with exercise therapy and insoles alone (SMD = 0.82 (95% CI: 0.24 to 1.41), $n = 49$) (Figure S10, supplementary material). Sensitivity analysis of laser dose categorisation The irradiation procedure by Darre et al.[66] was judged as a recommended laser dose, based on the reported dose parameters in the paper. However, the dose description is somewhat sparse and could be misinterpreted. If the study by Darre et al. was allocated to the unknown laser dose subgroup, the statistical heterogeneity would be eliminated in the recommended laser dose group and the estimated pain reduction would be increased to 21.12 mm VAS ((95% CI: 14.94 to 27.31), $I^2 = 0\%$, $n = 278$) versus placebo immediately after completed therapy (Figure S11, supplementary material). <i>Risk-of-bias within studies</i> Ten of the included trials were found to be of high methodological quality, and the remaining eight included trials were found to be of moderate methodological quality (Table 3). All the trials featured adequate randomisation. Allocation concealment was sufficient in 11 (61%) of the trials.
35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56	283 284 285 286 287 288 289 290 291 292 293 294 295 294 295 296 297 298 299 300	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), $I^2 = 69\%$, $n = 61$) (Figure S9, supplementary material). At follow-up 9 weeks after completed therapy, disability was significantly lowered by the recommended laser doses as an adjunct to stretching and insoles compared with exercise therapy and insoles alone (SMD = 0.82 (95% CI: 0.24 to 1.41), $n = 49$) (Figure S10, supplementary material). <i>Sensitivity analysis of laser dose categorisation</i> The irradiation procedure by Darre et al.[66] was judged as a recommended laser dose, based on the reported dose parameters in the paper. However, the dose description is somewhat sparse and could be misinterpreted. If the study by Darre et al. was allocated to the unknown laser dose subgroup, the statistical heterogeneity would be eliminated in the recommended laser dose group and the estimated pain reduction would be increased to 21.12 mm VAS ((95% CI: 14.94 to 27.31), $I^2 = 0\%$, $n = 278$) versus placebo immediately after completed therapy (Figure S11, supplementary material). <i>Risk-of-bias within studies</i> Ten of the included trials were found to be of high methodological quality, and the remaining eight included trials were found to be of high methodological quality (Table 3). All the trials featured adequate randomisation. Allocation concealment was sufficient in 11 (61%) of the trials. The groups were similar at baseline in 15 (83%) of the trials. The participants were blinded in nine
35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57	283 284 285 286 287 288 289 290 291 292 293 294 295 294 295 296 297 298 299 300 301	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), $I^2 = 69\%$, $n = 61$) (Figure S9, supplementary material). At follow-up 9 weeks after completed therapy, disability was significantly lowered by the recommended laser doses as an adjunct to stretching and insoles compared with exercise therapy and insoles alone (SMD = 0.82 (95% CI: 0.24 to 1.41), $n = 49$) (Figure S10, supplementary material). <i>Sensitivity analysis of laser dose categorisation</i> The irradiation procedure by Darre et al.[66] was judged as a recommended laser dose, based on the reported dose parameters in the paper. However, the dose description is somewhat sparse and could be misinterpreted. If the study by Darre et al. was allocated to the unknown laser dose subgroup, the statistical heterogeneity would be eliminated in the recommended laser dose group and the estimated pain reduction would be increased to 21.12 mm VAS ((95% CI: 14.94 to 27.31), $I^2 = 0\%$, $n = 278$) versus placebo immediately after completed therapy (Figure S11, supplementary material). <i>Risk-of-bias within studies</i> Ten of the included trials were found to be of high methodological quality, and the remaining eight included trials were found to be of high methodological quality. All the trials featured adequate randomisation. Allocation concealment was sufficient in 11 (61%) of the trials. The groups were similar at baseline in 15 (83%) of the trials. The participants were blinded in five (28%) of the trials, all of which were
35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58	283 284 285 286 287 288 289 290 291 292 293 294 295 294 295 296 297 298 299 300 301 302	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), $I^2 = 69\%$, $n = 61$) (Figure S9, supplementary material). At follow-up 9 weeks after completed therapy, disability was significantly lowered by the recommended laser doses as an adjunct to stretching and insoles compared with exercise therapy and insoles alone (SMD = 0.82 (95% CI: 0.24 to 1.41), $n = 49$) (Figure S10, supplementary material). <i>Sensitivity analysis of laser dose categorisation</i> The irradiation procedure by Darre et al.[66] was judged as a recommended laser dose, based on the reported dose parameters in the paper. However, the dose description is somewhat sparse and could be misinterpreted. If the study by Darre et al. was allocated to the unknown laser dose subgroup, the statistical heterogeneity would be eliminated in the recommended laser dose group and the estimated pain reduction would be increased to 21.12 mm VAS ((95% CI: 14.94 to 27.31), $I^2 = 0\%$, $n = 278$) versus placebo immediately after completed therapy (Figure S11, supplementary material). <i>Risk-of-bias within studies</i> Ten of the included trials were found to be of high methodological quality, and the remaining eight included trials were found to be of high methodological quality. All the trials featured adequate randomisation. Allocation concealment was sufficient in 11 (61%) of the trials. The groups were similar at baseline in 15 (83%) of the trials. The participants were blinded in five (28%) of the trials, all of which were placebo-controlled. The assessors were blinded in seven (39%) of the trials, all of which were
35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58	283 284 285 286 287 288 289 290 291 292 293 294 295 294 295 296 297 298 299 300 301	The disability results of the recommended laser doses applied as an adjunct to exercise therapy or stretching immediately after completed therapy favoured LLLT, but not significantly (SMD = 0.68 (95% CI: -0.49 to 1.85), $I^2 = 69\%$, $n = 61$) (Figure S9, supplementary material). At follow-up 9 weeks after completed therapy, disability was significantly lowered by the recommended laser doses as an adjunct to stretching and insoles compared with exercise therapy and insoles alone (SMD = 0.82 (95% CI: 0.24 to 1.41), $n = 49$) (Figure S10, supplementary material). <i>Sensitivity analysis of laser dose categorisation</i> The irradiation procedure by Darre et al.[66] was judged as a recommended laser dose, based on the reported dose parameters in the paper. However, the dose description is somewhat sparse and could be misinterpreted. If the study by Darre et al. was allocated to the unknown laser dose subgroup, the statistical heterogeneity would be eliminated in the recommended laser dose group and the estimated pain reduction would be increased to 21.12 mm VAS ((95% CI: 14.94 to 27.31), $I^2 = 0\%$, $n = 278$) versus placebo immediately after completed therapy (Figure S11, supplementary material). <i>Risk-of-bias within studies</i> Ten of the included trials were found to be of high methodological quality, and the remaining eight included trials were found to be of high methodological quality. All the trials featured adequate randomisation. Allocation concealment was sufficient in 11 (61%) of the trials. The groups were similar at baseline in 15 (83%) of the trials. The participants were blinded in five (28%) of the trials, all of which were

304 (78%) of the trials. An intention-to-treat analysis was used in 10 (56%) of the trials. A between305 group statistical comparison was performed in all the trials. Point measures and variability outcome
306 data were stated in 17 (94%) of the trial reports.

The lack of therapist and assessor blinding were the two most obvious methodological
 inadequacies. However, risk-of-bias subgroup analyses performed post-hoc revealed that there was
 no significant interaction between the effect estimates and the lack of blinding (Figures S12 and
 S13, supplementary material).

¹³ 311 *Risk-of-bias across studies (small study bias)*

In a random effects model, small and large trials are weighted relatively even when statistical heterogeneity is present. In a fixed effects model, the heterogeneity is ignored and will not influence the weights. Smaller studies in meta-analyses tend to show more positive results than larger 18 315 trials[82]. However, there was almost no difference between the pain results of the two meta-analysis models, indicating that no small study bias exists (Figures S14 and S15, supplementary material). Likewise, there was no obvious asymmetry in a funnel plot based on the same meta-analyses of pain, indicating that no small study bias was present (Figure S16, supplementary material). 24 320

Study ID	Item	num	ber									Tota	Qua
	1*	2	3	4	5	6	7	8	9	10	11	1	
Basford 1998[70]	+	+	-	+	+	5	+	+	-	+	+	7	Higl
Cinar 2017[71]	+	+	+	+	-		-	+	+	+	+	7	Hig
Cinar 2018[72]	+	+	+	+	-		-•	+	+	+	+	7	Hig
Darre 1994[66]	+	+	+	-	+	+		-	-	+	-	5	Moc e
Elsehrawy 2018[73]	+	+	-	+	-	-	- 4	+	-	+	+	5	Moo e
Kiritsi 2010[74]	+	+	+	+	+	+	+	- (+	+	8	Hig
Koteeswaran 2020[75]	+	+	-	+	-	-	-	+	+	+	+	6	Moo e
Lamba 2013[76]	+	+	-	+	+	-	-	+	-	+	+	6	Moo e
Liu 2014[64]	+	+	-	+	-	-	-	+	+	+	+	6	Moo e
Macias 2015[77]	+	+	+	+	+	-	+	+	+	+	+	9	Hig
Naterstad	+	+	+	+	+	+	+	+	+	+	+	10	Hig
Sanmak 2019[78]	+	+	+	+	-	-	-	+	+	+	+	7	Hig
Stergioulas 2003[65]	+	+	-	+	+	-	+	-	-	+	+	6	Moo e

Protected by co	
pyright, including for uses rela	Enseignement Superieur (ABES) .
r technologies.	

Stergioulas	+	+	+	+	+	-	-	-	+	+	+	8	High
2008[67]													
Tumilty	+	+	+	+	+	+	+	+	+	+	+	10	High
2008[68]													
Tumilty	+	+	+	+	+	+	+	+	+	+	+	10	High
2012[69]													
Ulusoy	+	+	-	+	-	-	-	+	-	+	+	5	Modera
2017[79]													e
Yüzer	+	+	+	+	-	-	-	-	-	+	+	5	Modera
2006[80]													e

*Item not included in the mean score.

** Naterstad et al. Efficacy of Low-level Laser Therapy as an addition to exercise and cryotherapy in chronic Achilles tendinopathy: a double-blinded randomised controlled trial

PEDro, Physiotherapy Evidence Database.

1. Eligibility criteria specified.

- 2. Random allocation.
- 3. Concealed allocation.
- 4. Groups similar at baseline.
- 5. Subject blinding.

- 6. Therapist blinding.
- 7. Assessor blinding.
- 8. Less than 15% dropout.
 - 9. Intention-to-treat analysis.
- 10. Between-group statistical comparisons.
- 11. Point measures and variability data.

DISCUSSION

We investigated the effectiveness of LLLT in tendon and aponeurosis disorders of the lower extremity. Our overall meta-analysis results demonstrated that pain and disability were statistically significantly reduced by LLLT compared with any control both immediately after completed therapy and in the follow-up period, that is, 4-12 weeks after completed therapy for pain and 4-8 38 341 weeks after completed therapy for disability.

Like in our previous meta-analysis of LLLT in knee osteoarthritis[40], we sub-grouped the included trials in the current review using the WALT treatment recommendations.[62, 63] Compared with placebo-control, the recommended laser doses in the current review generally had a larger pain-relieving effect than non-recommended laser both immediately after therapy and in the follow-up period. Similarly, the recommended laser doses had a significant pain-relieving effect as an adjunct to exercise therapy, stretching and insoles both immediately after completed therapy and in the follow-up period. Compared with other treatment modalities, the recommended laser doses were significantly superior, but only at follow-up and only as a pain treatment.

The minimal clinically important improvement (MCII) for pain expressed on the VAS or NRS has not been established for tendinopathy in the lower extremity [83], even though pain is a prominent feature of this condition. In plantar fasciitis, the MCII for VAS pain has been estimated 52 353 53 354 to be 8 mm for average pain[84], and our results are above this threshold in all comparisons.

54 355 As for disability, we found that LLLT overall had a small and significant effect both immediately after completed therapy and in the follow-up period. Compared with placebo, there were no significant effect of LLLT on disability immediately after completed therapy and at follow-ups. Only Cinar et al.[71] provided follow-up data on disability regarding LLLT as an add-on to exercise therapy. They found a large and significant positive effect on disability 12 weeks after

completed therapy, however, their results are based only on 49 participants[71], and thus this meta-analysis result should be interpreted with caution.

We were unable to dose categorise the study by Macias et al.[77], since they used a laser within the visible spectrum (635 nm), which is not mentioned in the WALT treatment guidelines. Light in the red wavelengths (600-700 nm) penetrates the tissue to a lesser extent than light with a wavelength of 700-1000 nm[85]. Macias et al. utilized a relatively low mean output power, but they stated that they irradiated the tissue for 600 seconds and achieved a significant pain reduction. The methodological quality of their trial[77] was categorised as high, with a PEDro score of 9.

Sanmak et al.[78] also used a laser within the red spectrum, but they applied a much smaller dose. Sanmak et al. [78] compared LLLT with ESWT in plantar fasciitis and found no difference between the groups regarding pain immediately after treatment, but an insignificant better result for ESWT 4 weeks after completed treatment. Comparing LLLT to ESWT, we would expect different effect-time profiles for pain alleviation, as the effect of ESWT might be greater at later time-points[86]. Sanmak et al.[78] applied LLLT in a circular motion on the insertion site of the plantar fascia for 60 seconds and along the fascia for another 60 seconds. They stated that they irradiated the tissue with 2 J/cm², which according to our calculation (Watt*seconds) corresponds to a relatively low mean output power of 18 mW/cm². Moving the laser probe during irradiation will 24 377 yield a smaller laser dose per treated cm², and larger movement will for instance reduce the energy delivered per treated cm². Additionally, the skin underneath the heel is thick[87], and thus absorbs a large percentage of the laser.

We did not identify any trials focusing on trochanter tendinopathy, peroneal or tibialis posterior tendinopathy. In a double-blinded randomised trial by Lögdberg-Andersson et al.[88], the effect of a 904 nm wavelength laser in participants with trochanteritis or myofascial pain was investigated. They found a significant positive effect compared with placebo on pain expressed on a VAS and with algometry, both at the end of treatment and four weeks after[88]. This trial was not 32 384 included in our review, since we were unable to isolate the participants of interest.

We were only able to identify two randomised controlled trials regarding the effect of LLLT compared with a control in patellar tendinopathy. Ashok et al.[89] have compared the effect of LLLT to that of therapeutic ultrasound in persons with patellar tendinopathy, and they found a statistically significant effect in favour of LLLT, both on pain reduction and function. However, it should be noted that this trial is small (n = 8) and only of moderate methodological quality. Another 39 390 40 391 LLLT trial by Meier et al. [90] included participants with both patellar tendinopathy (n = 58) and Achilles tendinopathy (n = 52). We omitted this trial, since it solely concerned the effects of an invisible (904 nm wavelength) laser versus a red (632 nm wavelength) laser. Meier et al. [90] stated that the red laser was placebo, but the laser dose applied in the sham procedure may possibly have had a photochemical effect. Both groups achieved a positive effect on a combined index of pain and function, favouring the 904 nm wavelength laser, but the report of the trial neither includes point effect estimates, nor variability data.

The presence and role of inflammation in chronic tendinopathy has been an ongoing debate in the last few decades. There is currently increased support that inflammation has a causal role in tendinopathy, where immune cells and molecular mediators are included as inflammatory components[91-93]. PGE₂ has been suggested to sustain inflammation and pain in human tendon disease[94]. In Achilles tendinopathy, a reduction of PGE₂ and a concurrent increased pain pressure threshold after LLLT were found in a double-blinded randomised clinical trial by Bjordal et al.[95], 54 403 55 404 where microdialysis of the tendon was performed in seven participants. The participants had 56 405 aggravated the symptoms through a pain inducing activity immediately prior to the examination. Only the immediate (105 minutes) response to LLLT was investigated in the trial, but the findings support the notion that LLLT may have an anti-inflammatory effect in Achilles tendinopathy.

3 4 Several authors of the included trials failed to adequately describe the laser dose parameters 408 5 used. A LLLT dose-response relationship has been established in systematic reviews of 409 6 410 tendinopathy[35-37] and osteoarthritis[40]. In the current review, some of the statistical 7 heterogeneity is plausibly due to the variation in laser doses applied. The statistical heterogeneity of 8 411 9 the dose subgroup analyses was generally lower than in the overall (any dose) analyses and this 412 10 413 indicates that the laser dose might be more important for the effect than the location of the 11 414 tendinopathy. The only study that caused noteworthy statistical heterogeneity in the dose subgroup 12 analysis with placebo-control was the one by Darre et al.[66]. Most of the pain and disability 415 13 416 analyses comparing LLLT with other interventions were based on trials of plantar fasciitis. These 14 analyses yielded a moderate level of statistical heterogeneity, and it may be explained by the 417 15 variation in control interventions. 16 418

The included trials had a moderate to high methodological quality (mean PEDro score = 7.1). Although therapist and assessor blinding lacked in many of the included studies, the lack of blinding was not significantly associated with higher effect estimates (supplementary material).

Future trials on the topic should include larger patient samples and directly compare the effectiveness of different LLLT parameters. Additionally, systematic reviews of LLLT should include dose-response investigations.

2425 425 Strengths and limitations of this study

26 426 This review was conducted in conformance with a detailed a priori published protocol, which 27 427 includes, for example, a plan for subgrouping the trials by laser dose. The review includes results 28 428 from two studies reported in non-English language[66, 80] and an unpublished study. The review 29 features meta-analyses with direct comparisons between LLLT and placebo LLLT, other 429 30 interventions and no intervention. Although only one reviewer extracted data from the included 430 31 32 431 trials, the extracted data was checked for correctness by another reviewer. 33

34 432 Implications for practice

The LLLT dose parameters were inadequately described in six (35%) of the trial articles. This

³⁶ 434 prohibited a comprehensive laser dose-response relationship investigation using the WALT

treatment recommendations.[38, 39] Since the laser doses identified as WALT recommended doses provided significantly positive results in most instances, we suggest adhering to these

provided significantly positive results in most instances, we suggest adher
 40 437 recommendations until further trials increase the precision of the analysis.

41 42 438 CONCLUSIONS

43 439 LLLT significantly reduces pain and disability in lower extremity tendinopathy and plantar fasciitis
 44 440 in the short and medium term. Long-term data was not available. Some uncertainty about the effect
 441 size remains due to wide confidence intervals and lack of larger trials.

47 442 Author contributions IFN and MBS wrote the PROSPERO protocol. IFN and MBS selected the 48 443 trials, with the involvement of JJ when necessary. IFN and MBS judged the risk-of-bias, with the 49 50 444 involvement of JJ when necessary. IFN and MBS extracted the data. IFN and MBS translated the non-English articles. IFN performed the analyses, under supervision by MBS. IFN, JJ, JMB, CC, 51 445 52 446 RABLM and MBS participated in interpreting of the results. IFN drafted the first version of the 53 447 manuscript, and subsequently revised it, based on comments by JJ, JMB, CC, RABLM and MBS. 54 448 All authors read and accepted the final version of the manuscript.

Acknowledgments None.

- **Funding** The Norwegian Fund for Post-Graduate Training for Physiotherapists funded this
- research, grant number 44944. No other specific grant from any funding agency in the public,
- commercial or not-for-profit sectors was received for this work. The corresponding author had full

BMJ Open

2 3									
4	453	200055	to all data in the study and had the final responsibility for the decision to submit for						
5	455	publication. Competing interests JMB and RABLM are former board members and prior presidents of the							
6	455	1							
7 8	456	World Association for Laser Therapy, a non-profit research organization from which they have							
9	457	never received funding, grants or fees. The other authors declared that they had no conflict of							
10		interests related to this work.							
11	459	Patient consent for publication Not required.							
12	460		I approval Not required.						
13	461		vailability statement The dataset for meta-analysis is available from the corresponding						
14	462		upon reasonable request. The corresponding author affirms that the manuscript is an honest,						
	463		te and transparent account of the study being reported; that no important aspects of the study						
	464		een omitted; and that any discrepancies from the study as planned (and, if relevant,						
	465		red) have been explained.						
19 20		U							
21	466	REFE	RENCES						
	467	1.	Riel, H., et al., Prevalence and incidence rate of lower-extremity tendinopathies in a Danish general						
	468		practice: a registry-based study. BMC Musculoskeletal Disorders, 2019. 20(1): p. 239.						
24 25	469	2.	Albers, S., J. Zwerver, and I. van den Akker-Scheek, 7 Incidence And Prevalence Of Lower Extremity						
26	470		<i>Tendinopathy In The General Population</i> . British Journal of Sports Medicine, 2014. 48 (Suppl 2): p.						
27	471	-	A5-A5.						
20		3.	Janssen, I., et al., <i>Investigating Achilles and patellar tendinopathy prevalence in elite athletics</i> .						
	473	4	Research in Sports Medicine, 2018. 26 (1): p. 1-12.						
	474 475	4.	Wang, J.H., M.I. Iosifidis, and F.H. Fu, <i>Biomechanical basis for tendinopathy</i> . Clin Orthop Relat Res,						
	475 476	5.	2006. 443 : p. 320-32. Magnusson, S.P. and M. Kjaer, <i>The impact of loading, unloading, ageing and injury on the human</i>						
	470	5.	tendon. J Physiol, 2019. 597(5): p. 1283-1298.						
34	478	6.	Prichasuk, S. and T. Subhadrabandhu, <i>The relationship of pes planus and calcaneal spur to plantar</i>						
35	479	0.	heel pain. Clin Orthop Relat Res, 1994(306): p. 192-6.						
36	480	7.	Rano, J.A., L.M. Fallat, and R.T. Savoy-Moore, <i>Correlation of heel pain with body mass index and</i>						
3/	481		other characteristics of heel pain. J Foot Ankle Surg, 2001. 40 (6): p. 351-6.						
39	482	8.	Riddle, D.L., et al., Risk factors for Plantar fasciitis: a matched case-control study. J Bone Joint Surg						
	483		Am, 2003. 85 (5): p. 872-7.						
41	484	9.	Taunton, J.E., et al., A retrospective case-control analysis of 2002 running injuries. Br J Sports Med,						
42	485		2002. 36 (2): p. 95-101.						
43	486	10.	Lemont, H., K.M. Ammirati, and N. Usen, <i>Plantar fasciitis: a degenerative process (fasciosis) without</i>						
44 45	487		inflammation. J Am Podiatr Med Assoc, 2003. 93 (3): p. 234-7.						
46	488	11.	Zhang, J., et al., Characterization of the structure, cells, and cellular mechanobiological response of						
47	489		<i>human plantar fascia.</i> J Tissue Eng, 2018. 9 : p. 2041731418801103.						
48	490	12.	van der Vlist, A.C., et al., Which treatment is most effective for patients with Achilles tendinopathy?						
	491		A living systematic review with network meta-analysis of 29 randomised controlled trials. Br J Sports						
	492		Med, 2020.						
	493	13.	Chan, K.M. and S.C. Fu, Anti-inflammatory management for tendon injuries - friends or foes? Sports						
52	494		Med Arthrosc Rehabil Ther Technol, 2009. 1(1): p. 23.						
53 54	495	14.	Aicale, R., et al., <i>Current pharmacological approaches to the treatment of tendinopathy</i> . Expert						
55	496	. –	Opinion on Pharmacotherapy, 2020. 21 (12): p. 1467-1477.						
56	497	15.	Jomaa, G., et al., A systematic review of inflammatory cells and markers in human tendinopathy.						
	498	4.6	BMC Musculoskeletal Disorders, 2020. 21 (1): p. 78.						
	499	16.	Duchman, K.R., et al., The Effect of Non-Steroidal Anti-Inflammatory Drugs on Tendon-to-Bone						
59 60	500		Healing: A Systematic Review with Subgroup Meta-Analysis. Iowa Orthop J, 2019. 39 (1): p. 107-119.						
00									

3			
4	501	17.	Paoloni, J.A., et al., Non-steroidal anti-inflammatory drugs in sports medicine: guidelines for
5 6	502		practical but sensible use. Br J Sports Med, 2009. 43(11): p. 863-5.
7	503	18.	Bussin, E.R., et al., Randomised controlled trial evaluating the short-term analgesic effect of topical
8	504		diclofenac on chronic Achilles tendon pain: a pilot study. BMJ Open, 2017. 7 (4): p. e015126.
9	505	19.	Heinemeier, K.M., et al., Effects of anti-inflammatory (NSAID) treatment on human tendinopathic
10	506		<i>tissue.</i> J Appl Physiol (1985), 2017. 123 (5): p. 1397-1405.
	507	20.	Astrom, M. and N. Westlin, No effect of piroxicam on achilles tendinopathy. A randomized study of
12	508		70 patients. Acta Orthop Scand, 1992. 63(6): p. 631-4.
13 14	509	21.	Bahla, N.E., J.; Patrono, C.; Baigent, C. et al., Vascular and upper gastrointestinal effects of non-
14	510		steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised
16	511		<i>trials.</i> The Lancet, 2013. 382 (9894): p. 769-779.
17	512	22.	Chung, H., et al., The nuts and bolts of low-level laser (light) therapy. Ann Biomed Eng, 2012. 40(2):
18	513		p. 516-33.
	514	23.	Bjordal, J.M., C. Couppe, and A.E. Ljunggren, Low Level Laser Therapy for Tendinopathy. Evidence of
	515		A Dose–Response Pattern. Physical Therapy Reviews, 2001. 6(2): p. 91-99.
	516	24.	Mussttaf, R.A., D.F.L. Jenkins, and A.N. Jha, Assessing the impact of low level laser therapy (LLLT) on
	517		<i>biological systems: a review.</i> International Journal of Radiation Biology, 2019. 95 (2): p. 120-143.
14	518	25.	Bjordal, J.M., et al., The anti-inflammatory mechanism of low level laser therapy and its relevance
25	519		for clinical use in physiotherapy. Physical Therapy Reviews, 2010. 15 (4): p. 286-293.
26	520	26.	Silveira, P.C., et al., Evaluation of mitochondrial respiratory chain activity in muscle healing by low-
	521		<i>level laser therapy</i> . J Photochem Photobiol B, 2009. 95 (2): p. 89-92.
	522	27.	Moriyama, Y., et al., In vivo study of the inflammatory modulating effects of low-level laser therapy
	523		on iNOS expression using bioluminescence imaging. Photochem Photobiol, 2005. 81(6): p. 1351-5.
	524	28.	Fillipin, L.I., et al., Low-level laser therapy (LLLT) prevents oxidative stress and reduces fibrosis in rat
	525		traumatized Achilles tendon. Lasers Surg Med, 2005. 37(4): p. 293-300.
32 33	526	29.	Chen, A.C., et al., Low-level laser therapy activates NF-kB via generation of reactive oxygen species
34	527		in mouse embryonic fibroblasts. PLoS One, 2011. 6(7): p. e22453.
35	528	30.	Luo, L., et al., Effects of low-level laser therapy on ROS homeostasis and expression of IGF-1 and
	529		TGF-81 in skeletal muscle during the repair process. Lasers Med Sci, 2013. 28(3): p. 725-34.
	530	31.	de Jesus, J.F., et al., Low-level laser therapy in IL-18, COX-2, and PGE2 modulation in partially
	531		injured Achilles tendon. Lasers Med Sci, 2015. 30(1): p. 153-8.
	532	32.	Marcos, R.L., et al., Infrared (810 nm) low-level laser therapy in rat achilles tendinitis: a consistent
	533		alternative to drugs. Photochem Photobiol, 2011. 87(6): p. 1447-52.
41 42	534	33.	Marcos, R.L., et al., Low-level laser therapy in collagenase-induced Achilles tendinitis in rats:
43	535		analyses of biochemical and biomechanical aspects. J Orthop Res, 2012. 30 (12): p. 1945-51.
44	536	34.	Frigo, L., et al., Low-Level Laser Irradiation (InGaAIP-660 nm) Increases Fibroblast Cell Proliferation
T J	537		and Reduces Cell Death in a Dose-Dependent Manner. Photomedicine and Laser Surgery, 2009.
	538		28 (S1): p. S-151-S-156.
	539	35.	Bjordal, J.M., C. Couppe, and A.E. Ljunggren, Low level laser therapy for tendinopathy. Evidence of a
	540		dose-response pattern. Physical Therapy Reviews 2001;6(2):91-99, 2001.
	541	36.	Haslerud, S., et al., The efficacy of low-level laser therapy for shoulder tendinopathy: a systematic
50	542		<i>review and meta-analysis of randomized controlled trials.</i> Physiother Res Int, 2015. 20 (2): p. 108-25.
51 52	543	37.	Tumilty, S., et al., Low level laser treatment of tendinopathy: a systematic review with meta-
53	544		analysis. Photomedicine and Laser Surgery 2010 Feb;28(1):3-16, 2010.
54	545	38.	WALT. Recommended treatment doses for Low Level Laser Therapy 780-860 nm wavelength. 2010a;
55	546		Available from: http://waltza.co.za/wp-content/uploads/2012/08/Dose_table_780-
56	547		860nm_for_Low_Level_Laser_Therapy_WALT-2010.pdf.
	548	39.	WALT. Recommended treatment doses for Low Level Laser Therapy 904 nm wavelength. 2010b;
	549		Available from: <u>http://waltza.co.za/wp-</u>
	550		content/uploads/2012/08/Dose_table_904nm_for_Low_Level_Laser_Therapy_WALT-2010.pdf.
60			

1			
2			
3			
4 5	551	40.	Stausholm, M.B., et al., Efficacy of low-level laser therapy on pain and disability in knee
6	552		osteoarthritis: systematic review and meta-analysis of randomised placebo-controlled trials. BMJ
7	553		Open, 2019. 9 (10): p. e031142.
8	554	41.	Stausholm, M.B., et al., Short- and Long-Term Effectiveness of Low-Level Laser Therapy Combined
9	555		with Strength Training in Knee Osteoarthritis: A Randomized Placebo-Controlled Trial. Journal of
10	556		Clinical Medicine, 2022. 11 (12): p. 3446.
11		42.	Huang, Y.Y., et al., Biphasic dose response in low level light therapy. Dose Response, 2009. 7(4): p.
12	550		358-83.
13	559	43.	Huang, YY., et al., Biphasic Dose Response in Low Level Light Therapy – an Update. Dose-Response,
14 15	560		2011. 9 (4): p. dose-response.11-009.Hamblin.
16	561	44.	Zein, R., W. Selting, and M.R. Hamblin, Review of light parameters and photobiomodulation
17	562		efficacy: dive into complexity. Journal of biomedical optics, 2018. 23(12): p. 1-17.
18	563	45.	Hamblin, M.R., Mechanisms and applications of the anti-inflammatory effects of
19	564		photobiomodulation. AIMS Biophys, 2017. 4(3): p. 337-361.
20	565	46.	Rhim, H.C., et al., Comparative Efficacy and Tolerability of Nonsurgical Therapies for the Treatment
21	566		of Midportion Achilles Tendinopathy: A Systematic Review With Network Meta-analysis. Orthop J
22	567		Sports Med, 2020. 8 (7): p. 2325967120930567.
23	568	47.	Cabrera Martimbianco, A.L., et al., Photobiomodulation with low-level laser therapy for treating
24 25	569		Achilles tendinopathy: a systematic review and meta-analysis [with consumer summary]. Clinical
25 26	570		Rehabilitation 2020 Jun;34(6):713-722, 2020.
20		48.	Wang, W., et al., Clinical efficacy of low-level laser therapy in plantar fasciitis: A systematic review
	572		and meta-analysis. Medicine (Baltimore), 2019. 98 (3): p. e14088.
	573	49.	Martimbianco, A.L.C., et al., Photobiomodulation with low-level laser therapy for treating Achilles
30	574		tendinopathy: a systematic review and meta-analysis. Clinical rehabilitation, 2020. 34 (6): p. 713-
31	575		722.
32	576	50.	Dos Santos, S.A., et al., Parameters and Effects of Photobiomodulation in Plantar Fasciitis: A Meta-
33	577		Analysis and Systematic Review. Photobiomodul Photomed Laser Surg, 2019. 37(6): p. 327-335.
34	578	51.	Salvioli, S., M. Guidi, and G. Marcotulli, The effectiveness of conservative, non-pharmacological
35	579		treatment, of plantar heel pain: A systematic review with meta-analysis. Foot (Edinb), 2017. 33 : p.
30	580		57-67.
	581	52.	Moher, D., et al., Preferred reporting items for systematic reviews and meta-analyses: the PRISMA
	582		statement. BMJ, 2009. 339 : p. b2535.
	583	53.	Wang, W., et al., Clinical efficacy of low-level laser therapy in plantar fasciitis: A systematic review
41	584		and meta-analysis. Medicine, 2019. 98 (3): p. e14088.
42	585	54.	Dos Santos, S.A., et al., Parameters and Effects of Photobiomodulation in Plantar Fasciitis: A Meta-
43	596	0.11	Analysis and Systematic Review. Photobiomodulation, photomedicine, and laser surgery, 2019.
44	50 7		37 (6): p. 327-335.
45	588	55.	de Morton, N.A., The PEDro scale is a valid measure of the methodological quality of clinical trials: a
	589	551	<i>demographic study</i> . Australian Journal of Physiotherapy, 2009. 55 (2): p. 129-133.
	590	56.	Moseley, A.M., et al., Reported quality of randomized controlled trials of physiotherapy
	591	501	<i>interventions has improved over time.</i> Journal of Clinical Epidemiology, 2011. 64 (6): p. 594-601.
50		57.	Higgins, J.P.T. and S. Green. Cochrane Handbook for Systematic Reviews of Interventions. 2011
51	593	57.	[cited 2015 3.12.]; Available from: http://handbook.cochrane.org/.
52	504	58.	Higgins, J.P. and S. Green. Cochrane Handbook for Systematic Reviews of Interventions. 2011;
53	505	50.	Available from: <u>http://handbook.cochrane.org/</u> .
54		59.	Thong, I.S.K., et al., The validity of pain intensity measures: what do the NRS, VAS, VRS, and FPS-R
55	596 597	59.	measure? Scand J Pain, 2018. 18 (1): p. 99-107.
	597 598	60	
	598 599	60.	Higgins, J.P. and S.G. Thompson, <i>Quantifying heterogeneity in a meta-analysis</i> . Stat Med, 2002. 21 (11): p. 1539-58.
	599 600	61.	21 (11): p. 1539-58. Higgins, J.P., et al., <i>Measuring inconsistency in meta-analyses.</i> Bmj, 2003. 327 (7414): p. 557-60.
60		01.	Tiggins, J.F., et al., weusuring inconsistency in meta-analyses. Dillj, 2005. 327 (7414). p. 557-60.

2 3			
3 4	(01	62	MALT Decomposed ad two streamt decose for low level leven the many 700,000 mm we we leve the world
5	601	62.	WALT. Recommended treatment doses for low level laser therapy 780-860 nm wavelength: world
6	602		association for laser therapy. 2010; Available from: <u>http://waltza.co.za/wp-</u>
7	603	62	content/uploads/2012/08/Dose_table_780-860nm_for_Low_Level_Laser_Therapy_WALT-2010.pdf
8	604	63.	WALT. Recommended treatment doses for low level laser therapy 904 nm wavelength: world
9	605		association for laser therapy. 2010; Available from: <u>http://waltza.co.za/wp-</u>
	606	<i>.</i>	content/uploads/2012/08/Dose_table_904nm_for_Low_Level_Laser_Therapy_WALT-2010.pdf
11 12		64.	Liu, XG., L. Cheng, and J.M. Song, <i>Effects of Low-Level Laser Therapy and Eccentric Exercises in the</i>
13	000	. -	Treatment of Patellar Tendinopathy. International Journal of Photoenergy, 2014. 2014.
14	00)	65.	Stergioulas, A., Effects of a 904 nm GaAs laser versus placebo in the treatment of patellar
15	610		<i>tendonitis.</i> Laser & Tecnology 2003. 13 (1-2): p. 21-26.
16	611	66.	Darre, E.M., Klokker, M., Lund, P., Rasmussen, J. D., Hansen, K., & Vedtofte, P. E., [Laser Therapy of
	612		Achilles Tendinitis]. Ugeskrift for Laeger, 1994. 156(45): p. 6680-6683.
	613	67.	Stergioulas, A., et al., Effects of low-level laser therapy and eccentric exercises in the treatment of
	614		recreational athletes with chronic achilles tendinopathy. Am J Sports Med, 2008. 36 (5): p. 881-7.
	615	68.	Tumilty, S., et al., Laser therapy in the treatment of Achilles tendinopathy: a pilot study.
	616		Photomedicine and Laser Surgery 2008 Feb;26(1):25-30, 2008.
22	617	69.	Tumilty, S., et al., Clinical effectiveness of low-level laser therapy as an adjunct to eccentric exercise
23 24	010		for the treatment of Achilles' tendinopathy: a randomized controlled trial. Archives of Physical
25	610		Medicine and Rehabilitation 2012 May;93(5):733-739, 2012.
26		70.	Basford, J.R., et al., A randomized controlled evaluation of low-intensity laser therapy: plantar
27	621		<i>fasciitis</i> . Arch Phys Med Rehabil, 1998. 79 (3): p. 249-54.
28	622	71.	Cinar, E., S. Saxena, and F. Uygur, Low-level laser therapy in the management of plantar fasciitis: a
	623		randomized controlled trial. Lasers in Medical Science 2018 Jul;33(5):949-958, 2018.
	624	72.	Cinar, E., S. Saxena, and F. Uygur, Combination therapy versus exercise and orthotic support in the
31			management of pain in plantar fasciitis: a randomized controlled trial. Foot & Ankle International
32	626		2018 Apr;39(4):406-414, 2018.
33 34	627	73.	Elsehrawy, G., et al., Extracorporeal Shock Wave Therapy versus Low-Level Laser Therapy in the
34 35			Management of Chronic Plantar Fasciitis. Suez Canal University Medical Journal, 2018. 21(2): p. 71-
36	629		81.
	630	74.	Kiritsi, O., et al., Ultrasonographic evaluation of plantar fasciitis after low-level laser therapy: results
38	631		of a double-blind, randomized, placebo-controlled trial. Lasers Med Sci, 2010. 25(2): p. 275-81.
39	632	75.	Koteeswaran, K., et al., Effectiveness of low level laser therapy versus ultrasound therapy with
40	633		plantar fascia streching in subjects with plantar fasciitis. Indian Journal of Public Health Research
41	634		and Development, 2020. 11 (1): p. 92-96.
42	0.2.2	76.	Lamba, D.T., M.; Pankaj, S., To Study the Characteristics and efficacy of 820 Nm GA-Al-As Diode
43	626		Laser for the Treatment of Plantar Fasciitis among Porters/Coolies in Kumaun Region, India: A
44 45	(27		Randomized Clinical. Indian Journal of Physiotherapy and Occupational Therapy - An International
45	638		Journal, 2013. 7 (4): p. 34-39.
	639	77.	Macias, D.M., et al., Low-Level Laser Therapy at 635 nm for Treatment of Chronic Plantar Fasciitis: A
	640		Placebo-Controlled, Randomized Study. J Foot Ankle Surg, 2015. 54 (5): p. 768-72.
	641	78.	Sanmak, O.D.Y., et al., Comparison of effects of low-level laser therapy and extracorporeal shock
50		70.	wave therapy in plantar fasciitis treatment: A randomized, prospective, single-blind clinical study.
51	012		Turkish Journal of Physical Medicine and Rehabilitation, 2019. 65 (2): p. 184-190.
52	644	79.	Ulusoy, A., L. Cerrahoglu, and S. Orguc, <i>Magnetic resonance imaging and clinical outcomes of laser</i>
53		75.	therapy, ultrasound therapy, and extracorporeal shock wave therapy for treatment of plantar
54	645 646		fasciitis: a randomized controlled trial. The Journal of Foot and Ankle Surgery 2017 Jul-
55	646 647		Aug;56(4):762-767, 2017.
	647 648	80.	Yüzer S, S.S., Gürçay E, Ünlü E, Çakcı A, Comparison of the effectiveness of laser therapy and steroid
	648 649	80.	injection in epin calcanei. Turk J Phys Med Rehabil, 2006. 52 : p. 68-71.
59			nijecilon ni epin culcullel. Turk j ritys Weu Kellabil, 2000. 32 . p. 06-71.
60			

651

652

653

654

14 659 15 660

18 662

5

6

7

8 9

10 655

11 656

12 657

13 658

14

16 ⁶⁶⁰ 17 ⁶⁶¹

19 663

20 664

21 665

22 666 23 667

24 25 ⁶⁶⁸

29 672

30 673

34 ⁶⁷⁶ 35 ⁶⁷⁷ 36 ⁶⁷⁸

40 682

41 683

47 48

49 689

50 690 51 691

52 691 692

53 693 54 694

55 695

56 696

60

81.	Stergioulas, A., et al., <i>Effects of low-level laser therapy and eccentric exercises in the treatment of recreational athletes with chronic Achilles tendinopathy.</i> The American Journal of Sports Medicine 2008 May;36(5):881-887, 2008.						
82.	IntHout, J., et al., <i>Small studies are more heterogeneous than large ones: a meta-meta-analysis.</i> Journal of Clinical Epidemiology, 2015. 68 (8): p. 860-869.						
83.	Murphy, M., et al., <i>Evaluating the progress of mid-portion Achilles tendinopathy during</i> <i>rehabilitation: a review of outcome measures for self- reported pain and function.</i> Int J Sports Phys Ther, 2018. 13 (2): p. 283-292.						
84.	Landorf, K.B., J.A. Radford, and S. Hudson, <i>Minimal Important Difference (MID) of two commonly used outcome measures for foot problems.</i> Journal of Foot and Ankle Research, 2010. 3 (1): p. 7.						
85.	Kwon, K., et al., <i>Enhancement of light propagation depth in skin: cross-validation of mathematical modeling methods.</i> Lasers Med Sci, 2009. 24 (4): p. 605-15.						
86.	Vulpiani, M.C., et al., <i>Extracorporeal shockwave therapy (ESWT) in Achilles tendinopathy. A long-</i> <i>term follow-up observational study</i> . J Sports Med Phys Fitness, 2009. 49 (2): p. 171-6.						
87.	Oltulu, P., et al., <i>Measurement of epidermis, dermis, and total skin thicknesses from six different body regions with a new ethical histometric technique.</i> Turkish Journal of Plastic Surgery, 2018. 26 (2): p. 56-61.						
88.	Lögdberg-Andersson M, M.S., Hazel Å., <i>Low level laser therapy of tendinitis and myofascial pain. A randomised double-blind controlled study.</i> Laser Therapy, 1997. 9 : p. 79-86.						
89.	Ashok, N., Raghul, S., Sivakumar, V.P.R, <i>Compare The Effects of Low-Level Laser and Ultrasonic</i> <i>Therapy in Subjects with Jumper's Knee</i> . International Journal of Research and Scientific Innovation, 2018. V (I).						
90. 91.	Meier, J.K., K., <i>Traitement laser de la tendinite</i> . Médecine et hygiène, 1988. 46 (1741): p. 907-911. Millar, N.L., B.J. Dean, and S.G. Dakin, <i>Inflammation and the continuum model: time to</i> <i>acknowledge the molecular era of tendinopathy</i> . British Journal of Sports Medicine, 2016. 50 (23): p.						
02	1486.						
92.	Dean, B.J.F., et al., <i>Are inflammatory cells increased in painful human tendinopathy? A systematic review.</i> British Journal of Sports Medicine, 2016. 50 (4): p. 216.						
93.	Mosca, M.J., et al., <i>Trends in the theory that inflammation plays a causal role in tendinopathy: a systematic review and quantitative analysis of published reviews.</i> BMJ Open Sport Exerc Med, 2018. 4 (1): p. e000332.						
94.	Bergqvist, F., et al., <i>Divergent roles of prostacyclin and PGE(2) in human tendinopathy</i> . Arthritis Res Ther, 2019. 21 (1): p. 74.						
95.	Bjordal, J.M., R.A. Lopes-Martins, and V.V. Iversen, <i>A randomised, placebo controlled trial of low level laser therapy for activated Achilles tendinitis with microdialysis measurement of peritendinous prostaglandin E2 concentrations</i> . Br J Sports Med, 2006. 40 (1): p. 76-80; discussion 76-80.						
Legend	ls:						
	1 Flow chart illustrating the trial identification process ysiotherapy Evidence Database.						
AT, Achil	2 Overall pain results immediately after completed therapy - LLLT versus any control les tendinopathy; CT, cryotherapy; ESWT, Extracorporeal Shock Wave Therapy; ET, exercise therapy; I, insoles; LLLT, Low-Level Laser PF, plantar fasciitis; PT, patellar tendinopathy; S, stretching; TU, Therapeutic Ultrasound.						
AT, Achil	3 Overall pain results at follow-ups - LLLT versus any control les tendinopathy; CT, cryotherapy; ESWT, Extracorporeal Shock Wave Therapy; ET, exercise therapy; I, insoles; LLLT, Low-Level Laser PF, plantar fasciitis; PT, patellar tendinopathy; S, stretching; TU, Therapeutic Ultrasound.						
Figure	Figure 4 Overall disability results immediately after completed therapy - LLLT versus any control						

vel Laser	
ellar	
ontrol nopathy;	
	Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

AT, Achilles tendinopathy; CT, cryotherapy; ESWT, Extracorporeal Shock Wave Therapy; ET, exercise therapy; I, insoles; LLLT, Low-Level Laser
 Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S = stretching; TU, Therapeutic Ultrasound.

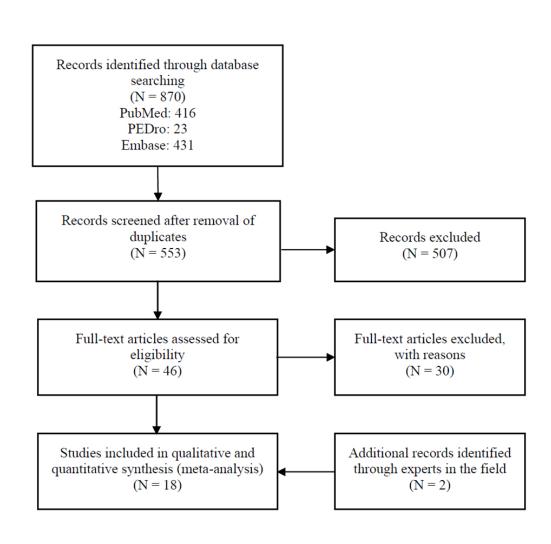
703 Figure 5 Overall disability results at follow-ups - LLLT versus any control

AT, Achilles tendinopathy; CT, cryotherapy; ET, exercise therapy; I, insoles; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S, stretching.
 706

⁷⁰⁷ Figure 6 Subgroup pain results immediately after completed therapy - LLLT versus placebo-control

AT, Achilles tendinopathy; CT, cryotherapy; ET, exercise therapy; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy;
 S, stretching.

to beet teries only



195x184mm (120 x 120 DPI)

BMJ Open: first published as 10.1136/bmjopen-2021-059479 on 28 September 2022. Downloaded from http://bmjopen.bmj.com/ on June 10, 2025 at Agence Bibliographique de I Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

		LLLT		c	ontrol			Mean Difference		Mean D	oifference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rand	om, 95% Cl	
1.1.1 LLLT vs placebo												
Darre 1994, LLLT vs placebo LLLT in AT	40.5	37.91	46	52	34.37	43	5.4%	-11.50 [-26.52, 3.52]		-	+	
Tumilty 2012, LLLT+ET vs placebo LLLT+ET in AT	6	17.1	20	9	7.45	20	7.8%	-3.00 [-11.17, 5.17]		_	+	
Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT	22.6	29.9	10		17.75	10	3.7%	5.40 [-16.15, 26.95]				
Basford 1998, LLLT vs placebo LLLT in PF		45.58	16	26.1		15	2.8%	8.30 [-18.50, 35.10]			<u> </u>	
Macias 2015, LLLT vs placebo LLLT in PF		22.49	37		14.56	32	7.6%	11.10 [2.27, 19.93]				
Naterstad, LLLT+ET+CT vs placebo LLLT+ET+CT in AT		29.18		11.54	35.09	21	4.1%	17.36 [-2.36, 37.08]				
Kiritsi 2010, LLLT vs placebo LLLT in PF	40	20.3	25	18	8.9	25	7.6%	22.00 [13.31, 30.69]				
Lamba 2013, LLLT+S vs placebo LLLT+S in PF	32	53	40	8.3	53	40	3.4%	23.70 [0.47, 46.93]				
Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT	24.8	25	26	0	25	26	5.9%	24.80 [11.21, 38.39]				-
Stergioulas 2003, LLLT vs placebo LLLT in PT Subtotal (95% CI)	35.5	71.04	18 258	6.4	12.39	17 249	2.0% 50.4%	29.10 [-4.24, 62.44] 11.48 [2.68, 20.28]		-		
Heterogeneity: Tau ² = 126.14; Chi ² = 32.84, df = 9 (P = 0.0	004). 12	- 700/	230			249	30.478	11.40 [2.00, 20.20]				
Test for overall effect: $Z = 2.56$ ($P = 0.01$)	JUU1); I*	= 73%										
1.1.2 LLLT vs no intervention												
Liu 2014, LLLT+ET vs ET in PT	62.86	10.4	7	46.43	10.69	7	6.8%	16.43 [5.38, 27.48]				
Cinar 2018, LLLT+S+I vs S+I in PF	38	24.9	24	20	25.28	17	5.3%	18.00 [2.39, 33.61]				
Cinar 2017, LLLT+S+I vs S+I in PF Subtotal (95% CI)	38.8	28.6	27 58	17.7	21.92	22 46	5.7% 17.7%	21.10 [6.95, 35.25] 18.15 [10.55, 25.76]			•	
Heterogeneity: Tau ² = 0.00; Chi ² = 0.26, df = 2 (P = 0.88);	l ² = 0%											
Test for overall effect: Z = 4.68 (P < 0.00001)												
1.1.3 LLLT vs other intervention												
Sanmak 2019, LLLT vs ESWT in PF		20.16	17		19.23	17	6.0%	0.00 [-13.24, 13.24]			+	
Liu 2014, LLLT vs ET in PT	52.86	12.2		46.43		7	6.4%	6.43 [-5.59, 18.45]		-	-	
Elsehrawy 2018, LLLT+S vs ESWT+S in PF		15.45	23	46	15.45	23	7.5%	11.00 [2.07, 19.93]				
Cinar 2018, LLLT+S+I vs ESWT+S+I in PF	38	24.9	24	16	23.1	25	5.9%	22.00 [8.54, 35.46]				
Koteeswaran 2020, LLLT+S vs TU+S in PF Subtotal (95% CI)	35.4	25.6	15 86	7.4	6.01	15 87	6.0% 31.9%	28.00 [14.69, 41.31] 13.23 [4.07, 22.39]			•	_
Heterogeneity: Tau ² = 70.74; Chi ² = 11.63, df = 4 (P = 0.02 Test for overall effect: Z = 2.83 (P = 0.005)	2); l² = 6	5%										
Total (95% CI)			402			382	100.0%	13.15 [7.82, 18.48]			•	
Heterogeneity: Tau ² = 77.51; Chi ² = 48.03, df = 17 (P < 0.0	0001)- 12	= 65%						-	-50 -	25	0 25	50

336x207mm (120 x 120 DPI)

Study or Subgroup	Mean	LLLT	Total	Mean	Control	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% C
2.1.1 LLLT vs placebo	Weall	30	Total	mean	30	Total	weight	IV, Kaliuolii, 95% Cl	IV, Randolli, 95% C
Turnilly 2012, LLLT+ET vs placebo LLLT+ET in AT	15	11.75	20	15	12.82	20	14.7%	0.00 [-7.62, 7.62]	
Naterstad, LLLT+ET+CT vs placebo LLLT+ET+CT in AT		36.46		22.99		20	7.0%	3.60 [-16.68, 23.88]	
Turnilty 2008. LLLT+ET vs placebo LLLT+ET in AT		30.40				10	5.9%		
Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT	17.9			20			8.8%	17.90 [1.41, 34.39]	
Basford 1998, LLLT vs placebo LLLT in PF						20			
Macias 2015. LLLT vs placebo LLLT in PF	29.6	62.57	15 37	19.4	61.92	13	2.0%		
						32	13.2%	24.20 [14.45, 33.95]	
Stergioulas 2003, LLLT vs placebo LLLT in PT Subtotal (95% CI)	60.6	88.57	18 140	17.3	21.87	17	2.3% 53.9%	43.30 [1.08, 85.52] 13.62 [2.18, 25.06]	
Heterogeneity: Tau ² = 130.26; Chi ² = 18.51, df = 6 (P = 0.0	06) 12-	60%	140			155	55.574	10.02 [2.10, 20.00]	-
Test for overall effect: $Z = 2.33$ (P = 0.02)	,03),1 =	00.00							
2.1.2 LLLT vs other intervention									
Sanmak 2019, LLLT vs ESWT in PF	20	32.64	17	30	39.76	17	5.5%	-10.00 [-34.45, 14.45]	
Ulusoy 2017, LLLT+ET+S vs ESWT+ET+S in PF	39.4	40.41	8	38.6	44.4	20	3.3%	0.80 [-33.30, 34.90]	
Ulusov 2017, LLLT+ET+S vs TU+ET+S in PF	39.4	40.41	9	31	31.8	17	4.0%	8.40 [-22.02, 38.82]	
Yuzer 2006, LLLT vs steroid injection in PF	48	22.91	26	38	23.32	30	11.5%	10.00 [-2.13, 22.13]	
Cinar 2018, LLLT+S+I vs ESWT+S+I in PF	44	24.9	24	22	35.13	25	8.6%		
Subtotal (95% CI)			84			109	32.8%	9.41 [-0.44, 19.26]	•
Heterogeneity: Tau ² = 21.59; Chi ² = 4.77, df = 4 (P = 0.31)	² = 169	6							
Test for overall effect: Z = 1.87 (P = 0.06)									
2.1.3 LLLT vs no intervention									
Cinar 2018, LLLT+S+I vs S+I in PF	44	26.05	24	27	29.17	17	8.4%	17.00 [-0.35, 34.35]	
Cinar 2017, LLLT+S+I vs S+I in PF	44.1	61.76	27	18.2	30.15	22	4.9%	25.90 [-0.58, 52.38]	
Subtotal (95% CI)			51			39	13.3%	19.67 [5.16, 34.18]	
Heterogeneity: Tau ² = 0.00; Chi ² = 0.30, df = 1 (P = 0.58);	² = 0%								
Test for overall effect: Z = 2.66 (P = 0.008)									
Total (95% CI)			275			281	100.0%	12.56 [5.69, 19.42]	•
Heterogeneity: Tau ² = 68.06; Chi ² = 25.08, df = 13 (P = 0.0	(2); $ ^2 = 4$	8%						-	-50 -25 0 25
Test for overall effect: Z = 3.59 (P = 0.0003)									-50 -25 0 25

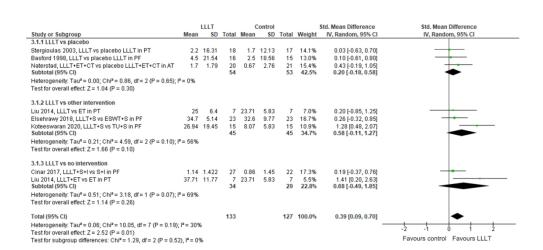
336x182mm (120 x 120 DPI)

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

1	
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	
40	
41	
42	
43	
44	
45	
46	
47	
48	
49	
50	
51	
52	
53	
54 55	
66	

58 59

60



338x153mm (120 x 120 DPI)

		LLLT		Control				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.1.1 LLLT vs placebo									
Macias 2015, LLLT vs placebo LLLT in PF	11.5	25.68	37	10.2	21	32	31.2%	0.05 [-0.42, 0.53]	
Naterstad, LLLT+ET+CT vs placebo LLLT+ET+CT in AT	2.03	1.72	20	1.44	3.11	21	19.0%	0.23 [-0.39, 0.84]	
Stergioulas 2003, LLLT vs placebo LLLT in PT	5.5	8.04	18	2.5	13.71	17	16.2%	0.26 [-0.40, 0.93]	
Basford 1998, LLLT vs placebo LLLT in PF	2.5	30.67	15	-7.5	22.96	13	12.9%	0.35 [-0.39, 1.10]	
Subtotal (95% CI)			90			83	79.3%	0.19 [-0.11, 0.49]	
Heterogeneity: Tau ² = 0.00; Chi ² = 0.56, df = 3 (P = 0.91); I ²	²= 0%								
Test for overall effect: Z = 1.22 (P = 0.22)									
4.1.2 LLLT vs no intervention									
Cinar 2017, LLLT+S+I vs S+I in PF	2.23	1.18	27	1.23	1.21	22	20.7%	0.82 [0.24, 1.41]	
Subtotal (95% CI)			27			22	20.7%	0.82 [0.24, 1.41]	
Heterogeneity: Not applicable									
Test for overall effect: Z = 2.75 (P = 0.006)									
Total (95% CI)			117			105	100.0%	0.32 [0.05, 0.59]	-
Heterogeneity: Tau ² = 0.00; Chi ² = 4.16, df = 4 (P = 0.39); I ²	= 4%							_	
Test for overall effect: Z = 2.29 (P = 0.02)									-1 -0.5 0 0.5 1

338x111mm (120 x 120 DPI)

Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.	Enseignement Superieur (ABES) .	MJ Open: first published as 10.1136/bmjopen-2021-059479 on 28 September 2022. Downloaded from http://bmjopen.bmj.com/ on June 10, 2025 at Agence Bibliographique de I
--	---------------------------------	---

Study or Subgroup	LLLT Mean SD	Total Mean	Control	Total We	Mean Difference eight IV, Random, 95% (Mean Difference Cl IV, Random, 95% Cl	
5.1.1 Recommended LLLT dose vs placebo Dare 1994, LLLT vs placebo LLLT in AT Tumity 2008, LLT+ET vs placebo LLLT+ET in AT Naterstad, LLLT+ET+CT vs placebo LLLT+ET+CT in AT Krinis 2010, LLLT vs placebo LLLT in PF Lamba 2013, LLLT+S vs placebo LLLT+IS in PF Stergioulas 2008, LLLT+ET vs placebo LLLT in AT Subtotal (95% CI) Heterogeneity: Tau* = 140.53; Chi* = 18.27, df = 6 (P = 0. Test for overail effect Z = 2.61 (P = 0.009)	40.5 37.91 22.6 29.9 28.9 29.18 40 20.3 32 53 24.8 25 35.5 71.04 006); I ^a = 67%	10 17.3 20 11.54 25 18 40 8.3 26 0	8 8.9 3 53	10 8 21 8 25 13 40 7 26 11 17 4	0.9% -11.50 [-26.52, 3.5] 8.2% 5.40 [-16.15, 26.9] 9.9% 17.36 [-2.36, 37.0] 8.9% 17.36 [-2.36, 37.0] 8.9% 22.00 [13.31, 30.6] 7.6% 23.70 [0.47, 46.9] 1.8% 24.80 [11.21, 38.3] 9.4% 14.98 [3.74, 26.2]		-
5.1.2 Non-recommended LLLT dose vs placebo Turnilly 2012, LLLT+ET vs placebo LLLT+ET in AT Subtold (195% C) Heterogenelly, Not applicable Test for overall effect Z = 0.72 (P = 0.47)	6 17.1	20 9 20	9 7.45	20 14 20 1	4.0% -3.00 [-11.17, 5.1] 4.0% -3.00 [-11.17, 5.1]	7]	
5.1.3 Unknown LLLT dose vs placebo Basford 1998, LLLT vs placebo LLLT in PF Macias 2015, LLLT vs placebo LLLT in PF Subtotal (95% Cl) Heterogeneity: Tau ² = 0.00, Chi ² = 0.04, df = 1 (P = 0.85), Testfor overall effect Z = 2.53 (P = 0.01)	34.4 45.58 19.8 22.49 ² = 0%	16 26.1 37 8.7 53	1 29.26 7 14.56	32 13	6.4% 8.30 [-18.50, 35.11 3.8% 11.10 [2.27, 19.93 0.2% 10.83 [2.44, 19.21	3]	
Total (95% CI) Heterogeneity: Tau ^a = 126.14; Chi ^a = 32.84, df = 9 (P = 0. Test for overall effect: Z = 2.56 (P = 0.01) Test for subgroup differences: Chi ^a = 8.38, df = 2 (P = 0.1		258		249 10	0.0% 11.48 [2.68, 20.28	8] -100 -50 0 50 Favours placebo Favours LLLT	
	336x1	66mn	n (12	20 x :	120 DPI)		
	336x1	66mn	n (12	20 x 3	120 DPI)		
	336x1	66mn	n (12	20 x 3	120 DPI)		
	336x1	66mn	n (12	20 x :	120 DPI)		
	336x1	66mn	n (12	20 x 3	120 DPI)		
	336x1	66mn	n (12	20 x 3	120 DPI)		
	336x1	66mn	n (12	20 x :	120 DPI)		
	336x1	66mn	n (12	20 x 3	120 DPI)		

 Supplemental digital content for the article:

Efficacy of low-level laser therapy in patients with lower extremity tendinopathy or plantar fasciitis: systematic review and meta-analysis of randomised controlled trials

Contents
PubMed database search string
Excluded full text articles
Supplementary figures
Figure S1 Pain at follow-ups 4-8 weeks after completed therapy - LLLT versus placebo
Figure S2 Subgroup pain results immediately after completed therapy - LLLT versus no intervention3
Figure S3 Pain at follow-ups 8 weeks after completed therapy - LLLT versus no intervention
Figure S4 Overall and subgroup pain results - LLLT versus other interventions
Figure S5 Pain at follow-ups 4-12 weeks after completed therapy - LLLT versus other interventions4
Figure S6 Disability at follow-ups 4-8 weeks after completed therapy - LLLT versus placebo
Figure S7 Disability immediately after completed therapy - LLLT versus placebo
Figure S8 Disability immediately after completed therapy - LLLT versus other interventions5
Figure S9 Disability immediately after completed therapy - LLLT versus no intervention
Figure S10 Disability at follow-up 9 weeks after completed therapy - LLLT versus no intervention5
Sensitivity analyses
Figure S11 Alternative LLLT dose subgrouping
Risk-of-bias within studies post-hoc analyses
Figure S12 Blinded versus unblinded assessor
Figure S13 Blinded versus unblinded therapist7
Risk-of-bias across studies - random versus fixed effects meta-analysis results of pain7
Figure S14 Random effects meta-analysis model7
Figure S15 Fixed effects meta-analysis model8
Figure S16 Funnel plot8

PubMed database search string

("Low-Level Light Therapy"[Mesh] OR LLLT[Title/Abstract] OR "low level"[Title/Abstract] OR "low power"[Title/Abstract] OR laser therap*[Title/Abstract] OR "laser acupuncture"[Title/Abstract] OR "low "HeNe"[Title/Abstract] OR "632 nm"[Title/Abstract] OR "Ga-Al-As"[Title/Abstract] OR "820 nm"[Title/Abstract] OR "830 nm"[Title/Abstract] OR "850 nm"[Title/Abstract] OR "GaAs"[Title/Abstract] OR "904 nm"[Title/Abstract] OR Photobiomodulation[Title/Abstract] OR phototherap*[Title/Abstract]) and ("Tendinopathy"[Mesh] or tendi*[Title/Abstract] or tendo*[Title/Abstract] or "plantar fasciitis"[Title/Abstract] or "Fasciitis, Plantar"[Mesh] or "Policeman's Heel"[Title/Abstract] or "Iliotibial Band Syndrome"[Mesh] or Iliopsoas tendi*[Title/Abstract] or "Achilles Tendon"[Mesh])

Excluded full text articles

10		
17	Author/Year/Reference	Reasons for exclusion
18	Abat et al. 2016 ¹	Impossible to isolate effect, combined treatments compared with other treatment
19	Aigner et al. 1996 ²	No control group
20	Ashok et al. 2018 ³	Lacks randomisation
21	Atik et al. 2018 ⁴	Commentary only
22	Bjordal et al. 2006⁵	Outcomes of interest not reported
23	Chang et al. 2015 ⁶	Outcomes of interest not reported
24	Cinar et al. 2013 ⁷	Conference paper only (author contacted)
25	Cinar et al. 2012 ⁸	Solely abstract available
26	Costantino et al. 2005 ⁹	Not LLLT, high intensity laser therapy
27	Coughlin et al. 2014 ¹⁰	Solely abstract available
28	Fernandes et al. 1991 ¹¹	Mixed population with unclear inclusion of diagnosis
29	Foley et al. 2016 ¹²	Not LLLT, light emitting diode therapy
30	Jastifer et al. 2014 ¹³	No control group
31	Lögdberg-Andersson et al. 1994 ¹⁴	Only pooled data on lower and upper extremity available
32	Mardh et al. 2016 ¹⁵	Not LLLT, high intensity laser therapy
33	Meier et al. 1988 ¹⁶	Outcomes of interest not reported
34	Morimoto et al. 2013 ¹⁷	No control group
35	Mulcahy et al. 1995 ¹⁸	Lacks credible control group, includes only 3 patients with tendinopathy
36	Notarnicola et al. 2014 ¹⁹	Not LLLT, high intensity laser therapy
37	Olivera et al. 2009 ²⁰	Animal study
38	Orellana-Molina et al. 2010 ²¹	Outcomes of interest not reported
39	Saxena et al. 2015 ²²	Not LLLT
40	Scott et al. 2011 ²³	Review
41	Siebert et al. 1987 ²⁴	Mixed population/diagnoses
42	Simunovic 1996 ²⁵	Narrative review
43	Suleymanoglu et al. 2014 ²⁶	Conference abstract
43	Takla et al. 2019 ²⁷	Used a combination of LLLT and light emitting diode therapy
44 45	Tumilty et al. 2015^{28}	Conference abstract
45 46	Tumilty et al. 2016 ²⁹	Not LLLT, high intensity laser therapy
40		

LLLT, low-level laser therapy.

Supplementary figures

Figure S1 Pain at follow-ups 4-8 weeks after completed therapy - LLLT versus placebo

4			LLLT		c	ontrol			Mean Difference	Mean Difference
5	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
	6.1.1 Recommended LLLT vs placebo									
6	Naterstad, LLLT+ET+CT vs placebo LLLT+ET+CT in AT	26.59	36.46	20	22.99	29.18	21	14.4%	3.60 [-16.68, 23.88]	
7	Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT	30.9		10	20	20	10		10.90 [-12.35, 34.15]	
/	Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT	17.9		20	0	26.6	20	16.9%		
8	Stergioulas 2003, LLLT vs placebo LLLT in PT Subtotal (95% CI)	60.6	88.57	18 68	17.3	21.87	17 68	5.7% 49.6%	43.30 [1.08, 85.52] 14.00 [2.81, 25.19]	•
9	Heterogeneity: Tau ² = 6.48; Chi ² = 3.14, df = 3 (P = 0.37);	I²= 5%								
10	Test for overall effect: Z = 2.45 (P = 0.01)									
	6.1.2 Non-recommended LLLT vs placebo									
11	Tumilty 2012, LLLT+ET vs placebo LLLT+ET in AT	15	11.75	20	15	12.82	20	23.4%	0.00 [-7.62, 7.62]	-+-
12	Subtotal (95% CI)			20			20	23.4%	0.00 [-7.62, 7.62]	•
	Heterogeneity: Not applicable									
13	Test for overall effect: Z = 0.00 (P = 1.00)									
14	6.1.3 Unknown LLLT dose vs placebo									
15	Basford 1998, LLLT vs placebo LLLT in PF		62.57	15		61.92	13		18.00 [-28.21, 64.21]	
	Macias 2015, LLLT vs placebo LLLT in PF	29.6	24.9	37	5.4	16	32	22.0%		
16	Subtotal (95% CI)			52			45	26.9%	23.94 [14.39, 33.48]	
17	Heterogeneity: Tau ² = 0.00; Chi ² = 0.07, df = 1 (P = 0.80); Test for overall effect: Z = 4.92 (P < 0.00001)	I* = U%								
18				4.40			422	400.0%	42 02 12 40 25 001	
	Total (95% CI)			140			133	100.0%	13.62 [2.18, 25.06]	
19	Heterogeneity: Tau ² = 130.26; Chi ² = 18.51, df = 6 (P = 0.0 Test for suprell effect: 7 = 2.32 (P = 0.02)	JU5); I* =	68%						-	-50 -25 0 25 50
20	Test for overall effect: Z = 2.33 (P = 0.02) Test for subgroup differences: Chi ² = 15.28, df = 2 (P = 0.	0006) 18	- 06 00	<u>د</u>						Favours placebo Favours LLLT
20	reactor aubgroup unicrences. Off = 15.26, ur = 2 (F = 0.	00000,1	- 00.97	0						

AT, Achilles tendinopathy; CT, cryotherapy; ESWT, Extracorporeal Shock Wave Therapy; ET, exercise therapy; I, insoles;

LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S, stretching; TU, Therapeutic Ultrasound.

Figure S2 Subgroup pain results immediately after completed therapy - LLLT versus no intervention

	1	LLLT		Control				Mean Difference	Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Rando	om, 95% Cl	
Liu 2014, LLLT+ET vs ET in PT	62.86	10.4	7	46.43	10.69	7	47.4%	16.43 [5.38, 27.48]				
Cinar 2018, LLLT+S+I vs S+I in PF	38	24.9	24	20	25.28	17	23.7%	18.00 [2.39, 33.61]				
Cinar 2017, LLLT+S+I vs S+I in PF	38.8	28.6	27	17.7	21.92	22	28.9%	21.10 [6.95, 35.25]				
Total (95% CI)			58			46	100.0%	18.15 [10.55, 25.76]			•	
Heterogeneity: Tau² = 0.00; Chi² = 0.26, df = 2 (P = 0.88); l² = 0% Test for overall effect: Z = 4.68 (P < 0.00001)									-50	-25	0 25	50
									-50	Favours control	Favours LLLT	50

ET, exercise therapy; I, insoles; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S, stretching.

Figure S3 Pain at follow-ups 8 weeks after completed therapy - LLLT versus no intervention

		LLLT		0	Control			Mean Difference					
Study or Subgroup	Mean	Mean SD Total Mean SD Total Weight IV, Random, 95% Cl			IV, Random, 95% Cl								
Cinar 2018, LLLT+S+I vs S+I in PF	44	26.05	24	27	29.17	17	70.0%	17.00 [-0.35, 34.35]					
Cinar 2017, LLLT+S+I vs S+I in PF	44.1	61.76	27	18.2	30.15	22	30.0%	25.90 [-0.58, 52.38]					
Total (95% CI)			51			39	100.0%	19.67 [5.16, 34.18]					
Heterogeneity: Tau ² = 0.00; Chi ² = 0.3	30, df = 1	I (P = 0.	.58); l² =	= 0%					-50	-25	0 25	50	
Test for overall effect: Z = 2.66 (P = 0	.008)								-50	Favours control		50	

ET, exercise therapy; I, insoles; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; S, stretching.

Figure S4 Overall and subgroup pain results - LLLT versus other interventions

2														
3			LLLT			ontrol			Mean Difference			ean Diffei		
	Study or Subgroup	Mean		Total	Mean	SD	Total	Weight	IV, Random, 95% C		IV,	Random,	95% CI	
4	9.3.1 Recommended LLLT dose vs other in	iterventi	on											
5	Liu 2014, LLLT vs ET in PT	52.86	12.2	7	46.43	10.69	7	20.2%	6.43 [-5.59, 18.45]					
6	Cinar 2018, LLLT+S+I vs ESWT+S+I in PF Subtotal (95% CI)	38	24.9	24 31	16	23.1	25 32	18.5% 38.7%	22.00 [8.54, 35.46] 13.91 [-1.34, 29.15]					
7	Heterogeneity: Tau ² = 78.83; Chi ² = 2.86, df =	= 1 (P = 0	.09); l²				-	00.170						
8	Test for overall effect: Z = 1.79 (P = 0.07)													
9	9.3.2 Unknown LLLT dose vs other interve	ntion												
10	Sanmak 2019, LLLT vs ESWT in PF	10	20.16	17	10	19.23	17	18.8%	0.00 [-13.24, 13.24]			-+-		
	Elsehrawy 2018, LLLT+S vs ESWT+S in PF	57	15.45	23	46	15.45	23	23.9%	11.00 [2.07, 19.93]			-		
11	Koteeswaran 2020, LLLT+S vs TU+S in PF	35.4	25.6	15	7.4	6.01	15	18.7%	28.00 [14.69, 41.31]					—
12	Subtotal (95% CI)			55			55	61.3%	12.88 [-1.29, 27.04]					
13	Heterogeneity: Tau ² = 120.11; Chi ² = 8.74, df	= 2 (P =	0.01); l [;]	² = 77%										
	Test for overall effect: Z = 1.78 (P = 0.07)													
14														
15	Total (95% CI)			86			87	100.0%	13.23 [4.07, 22.39]					
	Heterogeneity: Tau ² = 70.74; Chi ² = 11.63, df	= 4 (P =	0.02); l [:]	² = 66%						-50	-25		25	50
16	Test for overall effect: Z = 2.83 (P = 0.005)									00	Favours co	ontrol Fa	avours LLLT	00
17	Test for subgroup differences: Chi ² = 0.01, df	= 1 (P =	0.92), l ^a	² = 0%										
18														

ESWT, Extracorporeal Shock Wave Therapy; ET, exercise therapy; I, insoles; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S = stretching; TU, Therapeutic Ultrasound.

Figure S5 Pain at follow-ups 4-12 weeks after completed therapy - LLLT versus other interventions

25												
25			LLLT			Control			Mean Difference	Mean Diffe	rence	
26	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random,	, 95% CI	
27	10.3.1 Recommended LLLT dose vs other interve	ention										
	Ulusoy 2017, LLLT+ET+S vs ESWT+ET+S in PF	39.4	40.41	8	38.6	44.4	20	7.8%	0.80 [-33.30, 34.90]			
28	Ulusoy 2017, LLLT+ET+S vs TU+ET+S in PF	39.4	40.41	9	31	31.8	17	9.6%	8.40 [-22.02, 38.82]		•	-
29	Cinar 2018, LLLT+S+I vs ESWT+S+I in PF	44	24.9	24	22	35.13	25	26.1%	22.00 [5.00, 39.00]			-
	Subtotal (95% CI)			41			62	43.5%	15.90 [2.30, 29.51]	-		
30	Heterogeneity: Tau ² = 0.00; Chi ² = 1.48, df = 2 (P =	0.48); l ^a	'= 0%									
31	Test for overall effect: Z = 2.29 (P = 0.02)											
32	10.3.3 Unknown LLLT dose vs other intervention											
33	Sanmak 2019, LLLT vs ESWT in PF	20	32.64	17	30	39.76	17	14.3%	-10.00 [-34.45, 14.45]			
34	Yuzer 2006, LLLT vs steroid injection in PF Subtotal (95% CI)	48	22.91	26 43	38	23.32	30 47	42.2% 56.5%	10.00 [-2.13, 22.13] 2.93 [-15.80, 21.67]			
35	Heterogeneity: Tau ² = 103.01; Chi ² = 2.06, df = 1 (P	$2 = 0.15^{\circ}$	r I≧= 52					50.57	2.00[-10.00, 21.01]			
36	Test for overall effect: $Z = 0.31$ (P = 0.76)	,										
37	Total (95% CI)			84			109	100.0%	9.41 [-0.44, 19.26]			
38	Heterogeneity: Tau ² = 21.59; Chi ² = 4.77, df = 4 (P =	= 0.31);	l² = 16%	6						-50 -25 0	25	50
20	Test for overall effect: Z = 1.87 (P = 0.06)									Favours control F		50
39	Test for subgroup differences: Chi ² = 1.21, df = 1 (F	P = 0.27), l² = 17	².0%						1 415415 601401 1		

AT, Achilles tendinopathy; CT, cryotherapy; ESWT, Extracorporeal Shock Wave Therapy; ET, exercise therapy; I, insoles; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S, stretching; TU, Therapeutic Ultrasound.



45			LLLT		C	Control			Std. Mean Difference	Std. Mean Difference
46	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
	8.1.1 Recommended LLLT dose vs placebo									
7	Naterstad, LLLT+ET+CT vs placebo LLLT+ET+CT in AT	2.03	1.72	20	1.44	3.11	21	23.8%	0.23 [-0.39, 0.84]	
18	Stergioulas 2003, LLLT vs placebo LLLT in PT Subtotal (95% CI)	5.5	8.04	18 38	2.5	13.71	17 38	20.2% 44.0%	0.26 [-0.40, 0.93] 0.24 [-0.21, 0.70]	
9	Heterogeneity: Tau ² = 0.00; Chi ² = 0.01, df = 1 (P = 0.94); l ² :	= 0%								
0	Test for overall effect: Z = 1.06 (P = 0.29)									
1	8.1.3 Unknown LLLT dose vs placebo									
2	Macias 2015, LLLT vs placebo LLLT in PF	11.5	25.68	37	10.2	21	32	40.1%	0.05 [-0.42, 0.53]	_
	Basford 1998, LLLT vs placebo LLLT in PF Subtotal (95% CI)	2.5	30.67	15 52	-7.5	22.96	13 45	16.0% 56.0%	0.35 [-0.39, 1.10] 0.14 [-0.26, 0.54]	
3 4	Heterogeneity: Tau ² = 0.00; Chi ² = 0.44, df = 1 (P = 0.51); l ² =	= 0%		JŁ			45	50.0%	0.14 [-0.20, 0.34]	
	Test for overall effect: Z = 0.69 (P = 0.49)									
5	Total (95% CI)			90			83	100.0%	0.19 [-0.11, 0.49]	
б	Heterogeneity: Tau ² = 0.00; Chi ² = 0.56, df = 3 (P = 0.91); I ² :	= 0%								
7	Test for overall effect: Z = 1.22 (P = 0.22)									-1 -0.5 Ó 0.5 1 Favours placebo Favours LLLT
·/	Test for subgroup differences; Chi ² = 0.11, df = 1 (P = 0.73)	. I ^z = 09	6							Favours placebo Favours LLLT

Test for subgroup differences: Chi² = 0.11, df = 1 (P = 0.73), I² = 0%

AT, Achilles tendinopathy; CT, cryotherapy; ET, exercise therapy; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy.

Figure S7 Disability immediately after completed therapy - LLLT versus placebo

2			LLLT		(Control		:	Std. Mean Difference	Std. Mean Difference
2	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
3	7.1.1 Recommended LLLT dose vs placebo									
4	Stergioulas 2003, LLLT vs placebo LLLT in PT	2.2	16.31	18	1.7	12.13	17	33.0%	0.03 [-0.63, 0.70]	_
т _	Naterstad, LLLT+ET+CT vs placebo LLLT+ET+CT in AT	1.7	1.79	20	0.67	2.76	21	37.7%	0.43 [-0.19, 1.05]	+
5	Subtotal (95% CI)			38			38	70.8%	0.25 [-0.21, 0.70]	-
6	Heterogeneity: Tau ² = 0.00; Chi ² = 0.74, df = 1 (P = 0.39); l ²	= 0%								
0	Test for overall effect: Z = 1.07 (P = 0.29)									
7										
8	7.1.3 Unknown LLLT dose vs placebo									
	Basford 1998, LLLT vs placebo LLLT in PF	4.5	21.54	16	2.5	18.56	15	29.2%	0.10 [-0.61, 0.80]	
9	Subtotal (95% CI)			16			15	29.2%	0.10 [-0.61, 0.80]	
10	Heterogeneity: Not applicable									
	Test for overall effect: Z = 0.27 (P = 0.79)									
11	T-4-1/05% CIV						52	400.0%	0 20 1 0 40 0 501	
12	Total (95% CI)			54			53	100.0%	0.20 [-0.18, 0.58]	
	Heterogeneity: Tau ² = 0.00; Chi ² = 0.86, df = 2 (P = 0.65); l ²	= 0%								-2 -1 0 1 2
13	Test for overall effect: Z = 1.04 (P = 0.30)									Favours placebo Favours LLLT
	Test for subgroup differences: Chi ² = 0.12, df = 1 (P = 0.73)), I* = Us	%							

AT, Achilles tendinopathy; CT, cryotherapy; ET, exercise therapy; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy.

Figure S8 Disability immediately after completed therapy - LLLT versus other interventions

			-			-		-	-	
19			LLLT		С	ontrol			Std. Mean Difference	Std. Mean Difference
20	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
21	11.3.1 Recommended LLLT dose vs other in	terventi	on							
	Liu 2014, LLLT vs ET in PT	25	6.4	7	23.71	5.83	7	25.0%	0.20 [-0.85, 1.25]	
22	Subtotal (95% CI)			7			7	25.0%	0.20 [-0.85, 1.25]	
23	Heterogeneity: Not applicable									
24	Test for overall effect: Z = 0.37 (P = 0.71)									
25	11.3.2 Unknown LLLT dose vs other interve									
26	Elsehrawy 2018, LLLT+S vs ESWT+S in PF	34.7		23		9.77	23	41.8%	0.26 [-0.32, 0.85]	
	Koteeswaran 2020, LLLT+S vs TU+S in PF	26.94	19.45	15	8.07	5.83	15		1.28 [0.48, 2.07]	
27	Subtotal (95% CI)			38			38	75.0%	0.73 [-0.26, 1.72]	
28	Heterogeneity: Tau ² = 0.39; Chi ² = 4.07, df = 1	(P = 0.0	l4); l² = i	75%						
	Test for overall effect: Z = 1.45 (P = 0.15)									
29				45			45	400.00	0.505.044.4.071	
30	Total (95% CI)			45			45	100.0%	0.58 [-0.11, 1.27]	
31	Heterogeneity: Tau ² = 0.21; Chi ² = 4.59, df = 2	(P = 0.1	$(0); 1^{n} = 0$	06%						-2 -1 0 1 2
	Test for overall effect: Z = 1.66 (P = 0.10)									Favours control Favours LLLT
22	 Test for subgroup differences: Chi² = 0.53, df 	= 1 (P =	U.47), P	= 0%						

ET, exercise therapy; ESWT, Extracorporeal Shock Wave Therapy; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S, stretching; TU, Therapeutic Ultrasound.

Figure S9 Disability immediately after completed therapy - LLLT versus no intervention

38		LLLT		C	ontrol			Std. Mean Difference	Std. Mean Difference
39	Study or Subgroup	Mean SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
40	Cinar 2017, LLLT+S+I vs S+I in PF	1.14 1.422	27	0.86	1.45	22	60.2%	0.19 [-0.37, 0.76]	
40	Liu 2014, LLLT+ET vs ET in PT	37.71 11.77	7	23.71	5.83	7	39.8%	1.41 [0.20, 2.63]	
42	Total (95% CI)		34			29	100.0%	0.68 [-0.49, 1.85]	
43	Heterogeneity: Tau ² = 0.51; Chi ² = 3.		.07); l² =	= 69%					
44	Test for overall effect: Z = 1.14 (P = 0	1.26)							Favours no intervention Favours LLLT
45	ET, exercise therapy; I, inso	les; LLLT, I	Low-I	Level	Lase	r The	rapy; P	F, plantar fasciitis	; PT, patellar tendinopathy; S, stretching.

Figure S10 Disability at follow-up 9 weeks after completed therapy - LLLT versus no intervention

5			LLT		С	ontrol			Std. Mean Difference	Std. Mean Difference
)	Study or Subgroup	Mean	SD	Total	_	SD		Weight	IV, Random, 95% CI	IV, Random, 95% CI
)	Cinar 2017, LLLT+S+I vs S+I in PF	2.23	1.18	27	1.23	1.21	22	100.0%	0.82 [0.24, 1.41]	
	Total (95% CI)			27			22	100.0%	0.82 [0.24, 1.41]	
;	Heterogeneity: Not applicable Test for overall effect: Z = 2.75 (P = 0.	006)								-1 -0.5 0 0.5 1 Favours no intervention Favours LLLT

ET, exercise therapy; I, insoles; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S, stretching.

Sensitivity analyses

Allocating the study by Darre et al. 1994 to the unknown laser dose subgroup eliminates the statistical heterogeneity in the recommended laser dose subgroup and increases the estimate of placebo-controlled pain reduction to 21.12 mm VAS ((95% CI: 14.94 to 27.31), $I^2 = 0\%$, N = 278) immediately after completed therapy (Figure S11).

Figure S11 Alternative LLLT dose subgrouping

10			LLLT		c	Control			Mean Difference	Mean Difference
11	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% C	I IV, Random, 95% CI
	5.1.1 Recommended LLLT dose vs placebo									
12	Darre 1994, LLLT vs placebo LLLT in AT	40.5	37.91	46	52	34.37	43	0.0%	-11.50 [-26.52, 3.52]	
13	Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT	22.6	29.9	10	17.2	17.75	10	8.2%	5.40 [-16.15, 26.95]	
14	Naterstad, LLLT+ET+CT vs placebo LLLT+ET+CT in AT	28.9	29.18	20		35.09	21	8.9%	17.36 [-2.36, 37.08]	
	Kiritsi 2010, LLLT vs placebo LLLT in PF	40	20.3	25	18	8.9	25	13.8%	22.00 [13.31, 30.69]	
15	Lamba 2013, LLLT+S vs placebo LLLT+S in PF	32	53	40	8.3	53	40	7.6%	23.70 [0.47, 46.93]	
16	Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT	24.8	25	26	0		26	11.6%	24.80 [11.21, 38.39]	
17	Stergioulas 2003, LLLT vs placebo LLLT in PT Subtotal (95% CI)	35.5	71.04	18 139	6.4	12.39	17 139	4.9% 54.8%	29.10 [-4.24, 62.44] 21.12 [14.94, 27.31]	•
	Heterogeneity: Tau ² = 0.00; Chi ² = 2.77, df = 5 (P = 0.74);	l² = 0%								
18	Test for overall effect: Z = 6.69 (P < 0.00001)									
19										
20	5.1.2 Non-recommended LLLT dose vs placebo									
	Tumilty 2012, LLLT+ET vs placebo LLLT+ET in AT	6	17.1	20	9	7.45	20	14.0%	-3.00 [-11.17, 5.17]	
21	Subtotal (95% CI)			20			20	14.0%	-3.00 [-11.17, 5.17]	•
22	Heterogeneity: Not applicable									
	Test for overall effect: Z = 0.72 (P = 0.47)									
23	5.1.3 Unknown LLLT dose vs placebo									
24	Darre 1994, LLLT vs placebo LLLT in AT	40.5	37.91	46	50	34.37	43	10.9%	-11.50 [-26.52, 3.52]	
25	Basford 1998, LLLT vs placebo LLLT in PF		45.58	16		29.26	43	6.4%	8.30 [-18.50, 35.10]	
	Macias 2015, LLLT vs placebo LLLT in PF		22.49	37		14.56	32	13.8%	11.10 [2.27, 19.93]	_ _
26	Subtotal (95% CI)	10.0	22.45	99	0.7	14.00	90	31.1%	2.58 [-13.60, 18.75]	•
27	Heterogeneity: Tau ² = 135.31; Chi ² = 6.51, df = 2 (P = 0.04	(): $ ^2 = 6$	9%						. / .	Ť
	Test for overall effect: $Z = 0.31$ (P = 0.75)	,,								
28	,									
29	Total (95% CI)			258			249	100.0%	11.48 [2.68, 20.28]	\bullet
30	Heterogeneity: Tau ² = 126.14; Chi ² = 32.84, df = 9 (P = 0.0	0001); l²	= 73%							-100 -50 0 50 100
	Test for overall effect: Z = 2.56 (P = 0.01)									Favours placebo Favours LLLT
31	Test for subgroup differences: $Chi^2 = 22.55$, df = 2 (P < 0.0	0001), l²	= 91.1%							

AT, Achilles tendinopathy; CT, cryotherapy; ET, exercise therapy; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S, stretching.

Risk-of-bias within studies post-hoc analyses

Figure S12 Blinded versus unblinded assessor

40			LLLT			Control			Mean Difference	Mean Difference
41	Study or Subgroup	Mean	SD	Total	Mean		Total	Weight		IV, Random, 95% CI
42	17.1.1 Blinded assessor								, ,	
43	Tumilty 2012, LLLT+ET vs placebo LLLT+ET in AT	6	17.1	20	9	7.45	20	21.1%	-3.00 [-11.17, 5.17]	
	Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT	22.6		10	17.2		10	11.0%	5.40 [-16.15, 26.95]	•
44	Basford 1998, LLLT vs placebo LLLT in PF			16	26.1	29.26	15	8.4%	8.30 [-18.50, 35.10]	
45	Macias 2015, LLLT vs placebo LLLT in PF		22.49	37	8.7		32	20.6%	11.10 [2.27, 19.93]	
	Naterstad, LLLT+ET+CT vs placebo LLLT+ET+CT in AT	28.9		20	11.54		21	12.1%	17.36 [-2.36, 37.08]	
46	Kiritsi 2010, LLLT vs placebo LLLT in PF	40	20.3	25	18	8.9	25	20.7%	22.00 [13.31, 30.69]	
47	Stergioulas 2003, LLLT vs placebo LLLT in PT Subtotal (95% CI)	35.5	71.04	18 146	6.4	12.39	17 140	6.2% 100.0%	29.10 [-4.24, 62.44] 11.38 [1.85, 20.91]	
48	Heterogeneity: Tau ² = 94.57; Chi ² = 19.09, df = 6 (P = 0.00	04); I ² = 6	69%							-
49	Test for overall effect: Z = 2.34 (P = 0.02)									
50	17.1.3 Un-blinded assessor									
51	Darre 1994, LLLT vs placebo LLLT in AT	40.5	37.91	46	52	34.37	43	34.8%	-11.50 [-26.52, 3.52]	
	Lamba 2013, LLLT+S vs placebo LLLT+S in PF	32	53	40	8.3	53	40	29.7%	23.70 [0.47, 46.93]	
52	Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT	24.8	25	26	0	25	26	35.5%	24.80 [11.21, 38.39]	
53	Subtotal (95% CI)			112			109	100.0%	11.86 [-13.50, 37.21]	
	Heterogeneity: Tau ² = 422.80; Chi ² = 13.73, df = 2 (P = 0.0	001); l² =	85%							
54	Test for overall effect: Z = 0.92 (P = 0.36)									
55									-	
56										-50 -25 0 25 50
	Test for subgroup differences: $Chi^2 = 0.00$, $df = 1 (P = 0.92)$	7) $I^2 = 0^9$	1/2							Favours placebo Favours LLLT

Test for subgroup differences: $Chi^2 = 0.00$, df = 1 (P = 0.97), $I^2 = 0\%$

AT, Achilles tendinopathy; CT, cryotherapy; ET, exercise therapy; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S, stretching.

Figure S13 Blinded versus unblinded therapist

2			LLLT			ontrol			Mean Difference	Mean Difference
3	Study or Subgroup	Mean		Total	Mean		Total	Weight		IV, Random, 95% Cl
4	19.1.1 Blinded therapist							2		
5	Darre 1994, LLLT vs placebo LLLT in AT	40.5	37.91	46	52	34.37	43	19.9%	-11.50 [-26.52, 3.52]	
	Tumilty 2012, LLLT+ET vs placebo LLLT+ET in AT	6	17.1	20	9	7.45	20	23.6%	-3.00 [-11.17, 5.17]	
6	Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT	22.6	29.9	10			10	16.1%	5.40 [-16.15, 26.95]	
7	Naterstad, LLLT+ET+CT vs placebo LLLT+ET+CT in AT			20		35.09	21	17.1%	17.36 [-2.36, 37.08]	
8	Kiritsi 2010, LLLT vs placebo LLLT in PF Subtotal (95% CI)	40	20.3	25 121	18	8.9	25 119	23.4% 100.0%	22.00 [13.31, 30.69] 5.98 [-8.14, 20.10]	
9	Heterogeneity: Tau ² = 202.36; Chi ² = 24.10, df = 4 (P < 0.0	001); l²	= 83%							
10	Test for overall effect: $Z = 0.83$ (P = 0.41)									
11	19.1.3 Un-blinded therapist									
	Basford 1998, LLLT vs placebo LLLT in PF	34.4	45.58	16	26.1	29.26	15	6.6%	8.30 [-18.50, 35.10]	
12	Macias 2015, LLLT vs placebo LLLT in PF	19.8	22.49	37	8.7	14.56	32	55.3%	11.10 [2.27, 19.93]	-∎ -
13	Lamba 2013, LLLT+S vs placebo LLLT+S in PF	32	53	40	8.3	53	40	8.8%	23.70 [0.47, 46.93]	
	Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT	24.8	25	26	0	25	26	24.9%	24.80 [11.21, 38.39]	
14	Stergioulas 2003, LLLT vs placebo LLLT in PT	35.5	71.04	18	6.4	12.39	17	4.3%	29.10 [-4.24, 62.44]	<u> </u>
15	Subtotal (95% CI)			137			130	100.0%	16.21 [9.26, 23.16]	•
16	Heterogeneity: $Tau^2 = 2.44$; $Chi^2 = 4.13$, $df = 4$ (P = 0.39);	l² = 3%								
	Test for overall effect: Z = 4.57 (P < 0.00001)									
17									_	
18									_	-50 -25 0 25 50
19	Test for subgroup differences: $Chi^2 = 1.62$, df = 1 (P = 0.20)), I² = 38	3.4%							Favours placebo Favours LLLT

AT, Achilles tendinopathy; CT, cryotherapy; ET, exercise therapy; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S, stretching.

Risk-of-bias across studies - random versus fixed effects meta-analysis results of pain

There was almost no difference between the pain point estimates of the random and fixed effects models (pain immediately after the end of therapy), that is, 11.48 mm versus 10.21 mm VAS, indicating that no small study bias exists (Figures S14 and S15).

Figure S14 Random effects meta-analysis model

~~														
32			LLLT		c	ontrol			Mean Difference		Mean Dif	ference		
33 -	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% C	I	IV, Rando	m, 95% Cl		
34	5.1.1 Recommended LLLT dose vs placebo													
	Darre 1994, LLLT vs placebo LLLT in AT		37.91	46		34.37	43	10.9%	-11.50 [-26.52, 3.52]			-		
35	Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT	22.6	29.9	10	17.2		10	8.2%	5.40 [-16.15, 26.95]		-	•		
36	Naterstad, LLLT+ET+CT vs placebo LLLT+ET+CT in AT	28.9	29.18		11.54	35.09	21	8.9%	17.36 [-2.36, 37.08]		Ť	_		
	Kiritsi 2010, LLLT vs placebo LLLT in PF	40	20.3	25	18	8.9	25	13.8%	22.00 [13.31, 30.69]			_		
37	Lamba 2013, LLLT+S vs placebo LLLT+S in PF	32	53	40	8.3	53	40	7.6%	23.70 [0.47, 46.93]					
38	Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT Stergioulas 2003, LLLT vs placebo LLLT in PT	24.8	25 71.04	26 18	0 6.4	25 12.39	26 17	11.6% 4.9%	24.80 [11.21, 38.39] 29.10 [-4.24, 62.44]		1			
39	Subtotal (95% CI)	35.5	71.04	185	0.4	12.39	182	4.9% 65.7%	14.98 [3.74, 26.22]			<u>م</u>		
	Heterogeneity: Tau ² = 140.53; Chi ² = 18.27, df = 6 (P = 0.0	06); l ² =	67%											
40	Test for overall effect: Z = 2.61 (P = 0.009)													
41														
	5.1.2 Non-recommended LLLT dose vs placebo													
42	Tumilty 2012, LLLT+ET vs placebo LLLT+ET in AT Subtotal (95% CI)	6	17.1	20 20	9	7.45	20 20	14.0% 14.0%	-3.00 [-11.17, 5.17] -3.00 [-11.17, 5.17]			•		
43	Heterogeneity: Not applicable			20			20	14.070	-0.00[-11.11, 0.11]		•			
44	Test for overall effect: $Z = 0.72$ (P = 0.47)													
45	E 4 2 University I I I T door up place to													
46	5.1.3 Unknown LLLT dose vs placebo		45 50	10	00.4	~~~~	45	0.404	0.00/10 50.05 101					
	Basford 1998, LLLT vs placebo LLLT in PF		45.58	16	26.1	29.26	15	6.4%	8.30 [-18.50, 35.10]					
47	Macias 2015, LLLT vs placebo LLLT in PF Subtotal (95% CI)	19.8	22.49	37 53	8.7	14.56	32 47	13.8% 20.2%	11.10 [2.27, 19.93] 10.83 [2.44, 19.21]			٠		
48	Heterogeneity: Tau ² = 0.00; Chi ² = 0.04, df = 1 (P = 0.85);	² = 0%										•		
49	Test for overall effect: Z = 2.53 (P = 0.01)													
50	Total (95% CI)			258			249	100.0%	11.48 [2.68, 20.28]			•		
	Heterogeneity: Tau ² = 126.14; Chi ² = 32.84, df = 9 (P = 0.0	001); l²	= 73%							-100	-50 0) 5	0	100
51	Test for overall effect: Z = 2.56 (P = 0.01)										-50 0 Favours placebo		-	100
52	Test for subgroup differences: Chi ² = 8.38, df = 2 (P = 0.02), l² = 76	5.1%								area placebo	, arouro cce		

AT, Achilles tendinopathy; CT, cryotherapy; ET, exercise therapy; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S, stretching.

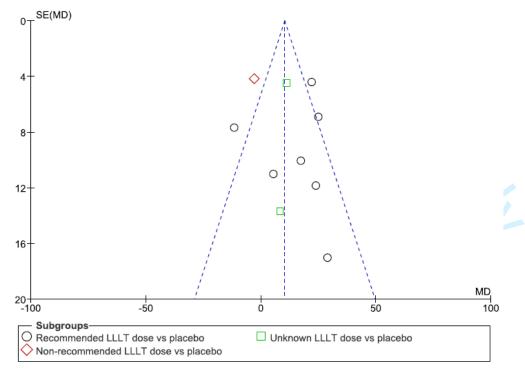
Figure S15 Fixed effects meta-analysis model

2			LLLT		Control			Mean Difference		Mean Difference
	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% C	IV, Fixed, 95% CI
3	5.1.1 Recommended LLLT dose vs placebo									
4	Darre 1994, LLLT vs placebo LLLT in AT		37.91	46		34.37	43		-11.50 [-26.52, 3.52]	
5	Tumilty 2008, LLLT+ET vs placebo LLLT+ET in AT	22.6	29.9	10		17.75	10	3.6%	5.40 [-16.15, 26.95]	
	Naterstad, LLLT+ET+CT vs placebo LLLT+ET+CT in AT		29.18	20		35.09	21	4.3%	17.36 [-2.36, 37.08]	
6	Kiritsi 2010, LLLT vs placebo LLLT in PF	40	20.3	25	18	8.9	25		22.00 [13.31, 30.69]	
7	Lamba 2013, LLLT+S vs placebo LLLT+S in PF Stergioulas 2008, LLLT+ET vs placebo LLLT+ET in AT	32 24.8	53 25	40 26	8.3 0	53 25	40 26	3.1%	23.70 [0.47, 46.93] 24.80 [11.21, 38.39]	
	Stergioulas 2003, LLLT vs placebo LLLT in PT		71.04	18	-	12.39	17		29.10 [-4.24, 62.44]	
8	Subtotal (95% CI)	35.5	71.04	185	0.4	12.00	182		16.39 [10.67, 22.11]	•
9	Heterogeneity: Chi ² = 18.27, df = 6 (P = 0.006); l ² = 67%									•
10	Test for overall effect: $Z = 5.62$ (P < 0.00001)									
11	5.1.2 Non-recommended LLLT dose vs placebo									
12	Tumilty 2012, LLLT+ET vs placebo LLLT+ET in AT	6	17.1	20	9	7.45	20	25.0%		
13	Subtotal (95% CI)			20			20	25.0%	-3.00 [-11.17, 5.17]	•
	Heterogeneity: Not applicable									
14	Test for overall effect: Z = 0.72 (P = 0.47)									
15	5.1.3 Unknown LLLT dose vs placebo									
16	Basford 1998, LLLT vs placebo LLLT in PF	34.4	45.58	16	26.1	29.26	15	2.3%	8.30 [-18.50, 35.10]	
	Macias 2015, LLLT vs placebo LLLT in PF	19.8	22.49	37	8.7	14.56	32	21.5%	11.10 [2.27, 19.93]	
17	Subtotal (95% CI)			53			47	23.8%	10.83 [2.44, 19.21]	◆
18	Heterogeneity: Chi ² = 0.04, df = 1 (P = 0.85); I ² = 0%									
19	Test for overall effect: Z = 2.53 (P = 0.01)									
20	Total (95% CI)			258			249	100.0%	10.21 [6.12, 14.30]	•
	Heterogeneity: Chi ² = 32.84, df = 9 (P = 0.0001); l ² = 73%									-100 -50 0 50 100
21	Test for overall effect: Z = 4.89 (P < 0.00001)									-100 -50 0 50 100 Favours placebo Favours LLLT
22	Test for subgroup differences: Chi ² = 14.54, df = 2 (P = 0.0	007), l²	= 86.2%	6						

AT, Achilles tendinopathy; CT, cryotherapy; ET, exercise therapy; LLLT, Low-Level Laser Therapy; PF, plantar fasciitis; PT, patellar tendinopathy; S, stretching.

Funnel plot of pain results immediately after completed therapy indicating that small study bias is absent (Figure S16).

Figure S16 Funnel plot



LLLT, Low-Level Laser Therapy; MD, mean difference; SE, standard error.

3

4

5

6

7

8 9

Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies	Enseignement Superieur (ABES)

References

- 1. Abat F, Sánchez-Sánchez JL, Martín-Nogueras AM, et al. Randomized controlled trial comparing the effectiveness of the ultrasound-guided galvanic electrolysis technique (USGET) versus conventional electro-physiotherapeutic treatment on patellar tendinopathy. J Exp Orthop 2016;3(1):34. doi: 10.1186/s40634-016-0070-4 [published Online First: 2016/11/18]
- 2. Aigner N, Fialka C, Weinstabl R, et al. Laser acupuncture for patellar tendinitis in athletes. [German]. Akupunktur 1996;24(1):11-14.
- 3. Ashok N, Raghul, S., Sivakumar, V.P.R. Compare The Effects of Low-Level Laser and Ultrasonic 10 Therapy in Subjects with Jumper's Knee. International Journal of Research and Scientific 11 Innovation 2018;V(I)
- 12 4. Atik OS. Photobiomodulation for Achilles Tendinopathy. Photomedicine and laser surgery 2018;36(1):1-13 2. doi: http://dx.doi.org/10.1089/pho.2017.4361 14
- 5. Bjordal JM, Lopes-Martins RA, Iversen VV. A randomised, placebo controlled trial of low level laser 15 therapy for activated Achilles tendinitis with microdialysis measurement of peritendinous 16 17 prostaglandin E2 concentrations. Br J Sports Med 2006;40(1):76-80; discussion 76-80. doi: 18 10.1136/bism.2005.020842 [published Online First: 2005/12/24]
- 19 6. Chang YP, Chiang H, Shih KS, et al. Effects of Therapeutic Physical Agents on Achilles Tendon 20 Microcirculation. J Orthop Sports Phys Ther 2015;45(7):563-9. doi: 10.2519/jospt.2015.5681 21 [published Online First: 2015/06/04] 22
- 7. Cinar E, Uygur F. Extracorporeal shock wave therapy versus low intensity laser therapy in the treatment 23 of heel pain. Annals of the Rheumatic Diseases Conference: Annual European Congress of 24 25 Rheumatology of the European League Against Rheumatism, EULAR 2013;72(no pagination) doi: 26 http://dx.doi.org/10.1136/annrheumdis-2013-eular.1709
- 27 8. Cinar E, Uygur F, Toprak Celenay S. The efficacy of low level laser therapy in the treatment of calcaneal 28 spur. Annals of the Rheumatic Disease Conference: Annual European Congress of Rheumatology of 29 the European League Against Rheumatism, EULAR 2012;71(no pagination) doi: 30 http://dx.doi.org/10.1136/annrheumdis-2012-eular.1438 31
- 9. Costantino C, Pogliacomi F, Vaienti E. Cryoultrasound therapy and tendonitis in athletes: a comparative 32 33 evaluation versus laser CO2 and t.e.ca.r. therapy. Acta Biomed 2005;76(1):37-41. [published Online 34 First: 2005/08/25] 35
- 10. Coughlin M, Stevens F, Doty J, et al. Evaluation of low-level laser therapy at 635nm for the treatment of 36 chronic plantar fasciitis: A placebo-controlled, randomized study. Lasers in surgery and medicine 37 2014;46:53-54. doi: http://dx.doi.org/10.1002/lsm.22229 38
- 11. Fernandes MS, Correia MG, Carvalho ML, et al. Laser therapy of inflammatory lesions of the soft parts 39 of the locomotor system. [Portuguese]. Acta medica portuguesa 1991;4(6):293-96. 40
- 41 12. Foley J, Vasily DB, Bradle J, et al. 830 nm light-emitting diode (led) phototherapy significantly reduced 42 return-to-play in injured university athletes: a pilot study. *Laser therapy* 2016;25(1):35-42. doi: 43 10.5978/islsm.16-OR-03 [published Online First: 2016/05/04] 44
- 13. Jastifer JR, Catena F, Doty JF, et al. Low-Level Laser Therapy for the Treatment of Chronic Plantar 45 Fasciitis: A Prospective Study. Foot & ankle international 2014;35(6):566-71. doi: 46 10.1177/1071100714523275 [published Online First: 2014/02/11] 47
- 48 14. Lögdberg-Andersson M MS, Hazel Å. . Low level laser therapy of tendinitis and myofascial pain. A 49 randomised double-blind controlled study. Laser Therapy 1997;9:79-86.
- 50 15. Mardh A, Lund I. High Power Laser for Treatment of Achilles Tendinosis - a Single Blind Randomized 51 Placebo Controlled Clinical Study. Journal of lasers in medical sciences 2016;7(2):92-8. doi: 52 10.15171/jlms.2016.16 [published Online First: 2016/06/23] 53
- 16. Meier JK, K. . Traitement laser de la tendinite. Médecine et hygiène 1988;46(1741):907-11. 54
- 17. Morimoto Y, Saito A, Tokuhashi Y. Low level laser therapy for sports injuries. Laser therapy 55 56 2013;22(1):17-20. [published Online First: 2013/10/25]
- 57 18. Mulcahy D, McCormack D, McElwain J, et al. Low level laser therapy: a prospective double blind trial 58 of its use in an orthopaedic population. Injury 1995;26(5):315-17. doi: https://doi.org/10.1016/0020-59 1383(95)00048-E 60

19. Notarnicola A, Maccagnano G, Tafuri S, et al. CHELT therapy in the treatment of chronic insertional Achilles tendinopathy. *Lasers Med Sci* 2014;29(3):1217-25. doi: 10.1007/s10103-013-1510-3 [published Online First: 2013/12/20]

- 20. Oliveira FS, Pinfildi CE, Parizoto NA, et al. Effect of low level laser therapy (830 nm) with different therapy regimes on the process of tissue repair in partial lesion calcaneous tendon. *Lasers in surgery and medicine* 2009;41(4):271-76. doi: <u>http://dx.doi.org/10.1002/lsm.20760</u>
- 21. Orellana Molina A, Hernandez Diaz A, Larrea Cox PJ, et al. Laser infrarrojo frente a acupuntura en el tratamiento del espolon calcaneo (Infrared laser versus acupuncture in the treatment of heel spurs) [Spanish]. *Revista de la Sociedad Espanola del Dolor 2010 Mar*;17(2):69-77 2010
- ¹⁰ [Spanish]. *Revisit de la Sociedad Espanoia del Dolor 2010 Mar*, 17(2):09-77 2010
 ¹¹ 22. Saxena A, St Louis M, Fournier M. Vibration and pressure wave therapy for calf strains: a proposed
 ¹² treatment. *Muscles Ligaments Tendons J* 2013;3(2):60-2. doi: 10.11138/mltj/2013.3.2.060 [published
 ¹³ Online First: 2013/07/28]
- Scott A, Backman LJ, Speed C. Tendinopathy: Update on Pathophysiology. *Journal of Orthopaedic & Sports Physical Therapy* 2015;45(11):833-41. doi: 10.2519/jospt.2015.5884
- 24. Siebert W, Seichert N, Siebert B, et al. What is the efficacy of "soft" and "mid" lasers in therapy of tendinopathies? A double-blind study. *Archives of Orthopaedic and Trauma Surgery 1987* 0ct;106(6):358-363 1987
- 25. Simunovic Z. Low level laser therapy with trigger points technique: A clinical study on 243 patients.
 Journal of Clinical Laser Medicine and Surgery 1996;14(4):163-67.
- 22
 26. Suleymanoglu T, Esmaeilzadeh S, Sen EI, et al. The effects of radial shock wave therapy and low level
 23
 24
 25
 26. Suleymanoglu T, Esmaeilzadeh S, Sen EI, et al. The effects of radial shock wave therapy and low level
 26. Suleymanoglu T, Esmaeilzadeh S, Sen EI, et al. The effects of radial shock wave therapy and low level
 26. Suleymanoglu T, Esmaeilzadeh S, Sen EI, et al. The effects of radial shock wave therapy and low level
 27. Interventional state of the state
- 27. Takla MKN, Rezk SSR. Clinical effectiveness of multi-wavelength photobiomodulation therapy as an
 adjunct to extracorporeal shock wave therapy in the management of plantar fasciitis: a randomized
 controlled trial. *Lasers in Medical Science* 2019 Apr;34(3):583-593 2019
- 28. Tumilty S, Baxter GD. Heavy load eccentric exercise for achilles tendinopathy; too much of a good thing? *Physiotherapy (United Kingdom)* 2015;101:eS1546-eS47. doi: http://dx.doi.org/org/10.1016/j.physio.2015.03.1541
- 29. Tumilty S, Mani R, Baxter GD. Photobiomodulation and eccentric exercise for Achilles tendinopathy: a
 randomized controlled trial. *Lasers in Medical Science 2016 Jan;31(1):127-135* 2016

Page 37 of 38

cted by co /bmjopen-2

PRISMA 20	009(Checklist	
Section/topic	#	Checklist item	Reported on page #
TITLE		g fo fo	
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT	<u>`</u>	s seic	
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data so results; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; fraiktions; conclusions and implications of key findings; systematic review registration number.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	2-3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participante, and study design (PICOS).	3
METHODS		g, · · · ·	
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address) and, if available, provide registration information including registration number.	3
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristica (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	3
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	3
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplemental
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic deview, and, if applicable, included in the meta-analysis).	3
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and	4

Data co Data items List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and | 4. 11 | simplifications made. Risk of bias in individual Describe methods used for assessing risk of bias of individual studies (including specification of whether this was 3-4 done at the study or outcome level), and how this information is to be used in any data synteesis. studies Summary measures State the principal summary measures (e.g., risk ratio, difference in means). Describe the methods of handling data and combining results of studies, if done, including a easures of Synthesis of results consistency (e.g., I²) for each meta-analysis. For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml de



PRISMA 2009 Checklist

cted by copyright /bmjopen-2021-05

		Page 1 of 2			
Section/topic	#	Checklist item	Reported on page #		
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	4		
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-receiptions), if done, indicating which were pre-specified.	9-10		
RESULTS		d to			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with screened, assessed for eligibility, and assessed for eligibility, and included in the review, with screened, assessed for eligibility, and included in the review, with a screened, assessed for eligibility, and assessed for eligibility, assessed for eligibility, and assessed for eligibility, and assessed for eligibility, assessed for eligibility, and assessed for eligibility, assessed for eligibility, and assessed for eligibility, assessed for eligibility, assessed for eligibility, assessed for eligi	4-5, supplemental		
Study characteristics	18	and provide the citations.	Table 1, Table 2		
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessmer been tem 12).	Table 3		
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot	Figur 2-6		
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	4-8		
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10		
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta egression [see Item 16]).	9, supplemental		
DISCUSSION	DISCUSSION				
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome sider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	11-13		
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., iscomplete retrieval of identified research, reporting bias).	12-13		
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13		
FUNDING	FUNDING				
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of date); role of funders for the systematic review.	13		

43 *From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The **PRISMA** Statement. PLoS Med 6(7): e1000097. 44 doi:10.1371/journal.pmed1000097 45 For peer reterministic many information where the present statement of the prese

