

Supplementary Materials

Title: A systematic review and network meta-analysis on the optimal wavelength of low-level light therapy (LLLT) in treating knee osteoarthritis symptoms

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Supplementary Table 1. Search strategies in four databases.

PubMed		Paper number
#1	"Osteoarthritis"[Mesh]	75,339
#2	OR "Osteoarthritis"[Title/Abstract] OR "Osteoarthritides"[Title/Abstract] OR "Osteoarthrosis"[Title/Abstract] OR "Osteoarthroses"[Title/Abstract] OR "Arthrosis"[Title/Abstract] OR "Arthroses"[Title/Abstract] OR "Degenerative Arthritides"[Title/Abstract] OR "Degenerative Arthritis"[Title/Abstract] OR "Osteoarthrosis Deformans"[Title/Abstract]	92,810
#3	"Low-Level Light Therapy"[Mesh] OR "Lasers, Semiconductor"[Mesh] OR "Laser Therapy"[Mesh] OR "Phototherapy"[Mesh]	110,595
#4	OR "Low-Level Light" [Title/Abstract] OR "Low Level Light" [Title/Abstract] OR "Photobiomodulation"[Title/Abstract] OR "LLLT"[Title/Abstract] OR "Low-Level Laser"[Title/Abstract] OR "Low Level Laser"[Title/Abstract] OR "Low-Power Laser"[Title/Abstract] OR "Low Power Laser"[Title/Abstract] OR "low-intensity laser"[Title/Abstract] OR "low intensity laser"[Title/Abstract] OR "Laser Biostimulation"[Title/Abstract] OR "Phototherapy"[Title/Abstract] OR "Light-Emitting Diode"[Title/Abstract] OR "Light Emitting Diode"[Title/Abstract] OR "laser therapy"[Title/Abstract] OR "high-intensity laser"[Title/Abstract]	32,774

	OR "high intensity laser"[Title/Abstract] OR "high-power laser"[Title/Abstract] OR "high power laser"[Title/Abstract] OR "high-level laser"[Title/Abstract] OR "high level laser"[Title/Abstract]	
#5	"randomized controlled trial"[Publication Type] OR "controlled clinical trial"[Publication Type] OR "randomized"[Title/Abstract] OR "randomised"[Title/Abstract] OR "randomization"[Title/Abstract] OR "randomisation"[Title/Abstract] OR "randomly"[Title/Abstract] OR "placebo"[Title/Abstract] OR "trial"[Title/Abstract]	1,668,089
(#1 OR #2) AND (#3 OR #4) AND #5	((("Osteoarthritis"[Mesh] OR "Osteoarthritis"[Title/Abstract] OR "Osteoarthritides"[Title/Abstract] OR "Osteoarthrosis"[Title/Abstract] OR "Osteoarthroses"[Title/Abstract] OR "Arthrosis"[Title/Abstract] OR "Arthroses"[Title/Abstract] OR "Degenerative Arthritides"[Title/Abstract] OR "Degenerative Arthritis"[Title/Abstract] OR "Osteoarthrosis Deformans"[Title/Abstract])) AND ("Low-Level Light Therapy"[Mesh] OR "Lasers, Semiconductor"[Mesh] OR "Laser Therapy"[Mesh] OR "Phototherapy"[Mesh] OR "Low-Level Light"[Title/Abstract] OR "Low Level Light"[Title/Abstract] OR "Photobiomodulation"[Title/Abstract] OR "LLLT"[Title/Abstract] OR "Low-Level Laser"[Title/Abstract] OR "Low Level Laser"[Title/Abstract] OR "Low-Power Laser"[Title/Abstract] OR "Low Power Laser"[Title/Abstract] OR "low-intensity laser"[Title/Abstract] OR "low intensity laser"[Title/Abstract] OR "Laser Biostimulation"[Title/Abstract] OR "Phototherapy"[Title/Abstract] OR "Light-Emitting Diode"[Title/Abstract] OR "Light Emitting Diode"[Title/Abstract] OR "laser therapy"[Title/Abstract] OR "high-intensity laser"[Title/Abstract] OR "high intensity laser"[Title/Abstract] OR "high-	144

	power laser"[Title/Abstract] OR "high power laser"[Title/Abstract] OR "high-level laser"[Title/Abstract] OR "high level laser"[Title/Abstract])) AND ("randomized controlled trial"[Publication Type] OR "controlled clinical trial"[Publication Type] OR "randomized"[Title/Abstract] OR "randomised"[Title/Abstract] OR "randomization"[Title/Abstract] OR "randomisation"[Title/Abstract] OR "randomly"[Title/Abstract] OR "placebo"[Title/Abstract] OR "trial"[Title/Abstract])	
Embase		
#1	'low level laser therapy'/exp OR 'phototherapy'/exp	110,429
#2	'light therapy':ab,ti OR 'low level light':ab,ti OR 'photobiomodulation':ab,ti OR 'lllt':ab,ti OR 'low-level laser':ab,ti OR 'low level laser therapy':ab,ti OR 'low-power laser':ab,ti OR 'low power laser':ab,ti OR 'low-intensity laser':ab,ti OR 'low intensity laser':ab,ti OR 'laser biostimulation':ab,ti OR 'laser phototherapy':ab,ti OR 'Light-Emitting Diode':ab,ti OR 'Light Emitting Diode':ab,ti OR 'laser therapy':ab,ti OR 'high-intensity laser':ab,ti OR 'high intensity laser':ab,ti OR 'high-power laser':ab,ti OR 'high power laser':ab,ti OR 'high-level laser':ab,ti OR 'high level laser':ab,ti	27,476
#3	'osteoarthritis'/exp	158,498
#4	('osteoarthritis' OR osteoarthritis:ti,ab,kw OR osteoarthritides:ti,ab,kw OR osteoarthrosis:ti,ab,kw OR osteoarthroses:ti,ab,kw OR arthrosis:ti,ab,kw OR arthroses:ti,ab,kw) AND [english]/lim	116,579
#5	'randomized controlled trial'/exp OR 'randomized controlled trial':ti,ab,it OR 'randomized':ti,ab,it OR 'randomised':ti,ab,it OR 'randomization':ti,ab,it OR 'randomisation':ti,ab,it OR 'rct':ti,ab,it OR 'randomly':ti,ab,it OR	1,878,522

	'placebo':ti,ab,it	
(#1 OR #2) AND (#3 OR #4) AND #5		238
Web of Science		
#1	(((TS=(osteoarthritis)) OR TI=("osteoarthritis" OR "Osteoarthritis" OR "Osteoarthritis" OR "Osteoarthritis" OR "Arthrosis" OR "Arthroses" OR "Degenerative Arthritis" OR "Degenerative Arthritis" OR "Osteoarthritis Deformans"))) OR AB=("osteoarthritis" OR "Osteoarthritis" OR "Osteoarthritis" OR "Osteoarthritis" OR "Arthrosis" OR "Arthroses" OR "Degenerative Arthritis" OR "Degenerative Arthritis" OR "Osteoarthritis Deformans"))) OR AK=("osteoarthritis" OR "Osteoarthritis" OR "Osteoarthritis" OR "Osteoarthritis" OR "Arthrosis" OR "Arthroses" OR "Degenerative Arthritis" OR "Degenerative Arthritis" OR "Osteoarthritis Deformans"))	117,350
#2	(((TS=("Low-Level Light Therapy" OR "Lasers, Semiconductor" OR "Laser Therapy" OR "Phototherapy" OR "Light-Emitting Diode" OR "Light Emitting Diode"))) OR TI=("Low-Level Light" OR "Low Level Light" OR "Photobiomodulation" OR "LLLT" OR "Low-Level Laser" OR "Low Level Laser" OR "Low-Power Laser" OR "Low Power Laser" OR "Low-intensity Laser" OR "Low intensity Laser" OR "Laser Biostimulation" OR "Laser	1,024,838

	Phototherapy" OR "Laser" OR "Light-Emitting Diode" OR "Light Emitting Diode" OR "High-Level Light" OR " High Level Light" OR " High-Level Laser" OR "High Level Laser" OR "High-Power Laser" OR "High Power Laser" OR "High-intensity Laser" OR "High intensity Laser")) OR AB=("Low-Level Light" OR "Low Level Light" OR "Photobiomodulation" OR "LLLT" OR "Low-Level Laser" OR "Low Level Laser" OR "Low-Power Laser" OR "Low Power Laser" OR "Low-intensity Laser" OR "Low intensity Laser" OR "Laser Biostimulation" OR "Laser Phototherapy" OR "Laser" OR "Light-Emitting Diode" OR "Light Emitting Diode" OR "High-Level Light" OR " High Level Light" OR " High-Level Laser" OR "High Level Laser" OR "High-Power Laser" OR "High Power Laser" OR "High-intensity Laser" OR "High intensity Laser")) OR AK=("Low-Level Light" OR "Low Level Light" OR "Photobiomodulation" OR "LLLT" OR "Low-Level Laser" OR "Low Level Laser" OR "Low-Power Laser" OR "Low Power Laser" OR "Low-intensity Laser" OR "Low intensity Laser" OR "Laser Biostimulation" OR "Laser Phototherapy" OR "Laser" OR "Light-Emitting Diode" OR "Light Emitting Diode" OR "High-Level Light" OR " High Level Light" OR " High-Level Laser" OR "High Level Laser" OR "High-Power Laser" OR "High Power Laser" OR "High-intensity Laser" OR "High intensity Laser")	
#3	TS=(Randomized controlled trial)	498,279
#1 AND #2 #3		119
Cochrane Library		

#1	MeSH descriptor: [Osteoarthritis] explode all trees	9570
#2	("Osteoarthritis" OR "Osteoarthritides" OR "Osteoarthrosis" OR "Osteoarthroses" OR "Arthrosis" OR "Arthroses" OR "Degenerative Arthritides" OR "Degenerative Arthritis" OR "Osteoarthrosis Deformans"):ti,ab,kw	22,113
#3	MeSH descriptor: [Low-Level Light Therapy] explode all trees OR MeSH descriptor: [Lasers, Semiconductor] explode all trees OR MeSH descriptor: [Laser Therapy] explode all trees OR MeSH descriptor: [Phototherapy] explode all trees	7,927
#4	("Low-Level Light" OR "Low Level Light" OR "Photobiomodulation" OR "LLLT" OR "Low-Level Laser" OR "Low Level Laser" OR "Low-Power Laser" OR "Low Power Laser" OR "Low-intensity Laser" OR "Low intensity Laser" OR "Laser Biostimulation" OR "Phototherapy" OR "Laser Phototherapy" OR "Laser" OR "Light-Emitting Diode" OR "Light Emitting Diode" OR "High-Level Laser" OR "High Level Laser" OR "High-Power Laser" OR "High Power Laser" OR "High-intensity Laser" OR "High intensity Laser"):ti,ab,kw	26,087
	(#1 OR #2) AND (#3 OR #4)	273

Supplementary Table 2 GRADE certainty of evidence for LLLT on knee pain.

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	LLLT	sham LLLT	Relative (95% CI)	Absolute (95% CI)	
Conventional meta-analysis (Overall LLLT compare with sham LLLT)											
13	randomised trials	serious ^a	serious ^b	not serious ^c	not serious	publication bias strongly suspected strong association ^c	342	300	SMD 0.96 SD higher (0.31 higher to 1.61 higher)	⊕⊕○○ Low	
NMA estimate on MWL vs. Sham											
4	randomised trials	not serious ^a	not serious	very serious ^d	serious ^c	none	125	120	SMD 0.83 SD higher (-0.06 lower to 1.72 higher)	⊕○○○ Very low	
NMA estimate on L2 vs. Sham											
3	randomised trials	not serious	serious ^f	very serious ^d	not serious	strong association	84	81	SMD 1.42 SD higher (0.31 higher to 2.53 higher)	⊕⊕○○ Low	
NMA estimate on L1 vs. Sham											
7	randomised trials	serious ^a	serious ^g	very serious ^d	not serious	strong association	133	130	SMD 0.81 SD higher (0.11 higher to 1.50 higher)	⊕○○○ Very low	

CI: confidence interval; SMD: standardised mean difference; LLLТ: low-level light therapy; L1: 785-850 nm LLLТ; L2: 904-905 nm LLLТ; MWL: multi-wavelength LLLТ; Sham: sham LLLТ; NMA: network meta-analysis; GRADE: grading of recommendations, assessment, development, and evaluation

Explanations: a. One study is high risk due to missing outcome data; b. I^2 is 86%; c. P-value for Egger regression test of funnel plot asymmetry is 0.0376; d. From network meta-analysis
e. 95% CI includes 0; f. I^2 is 95%; g. I^2 is 88.8%

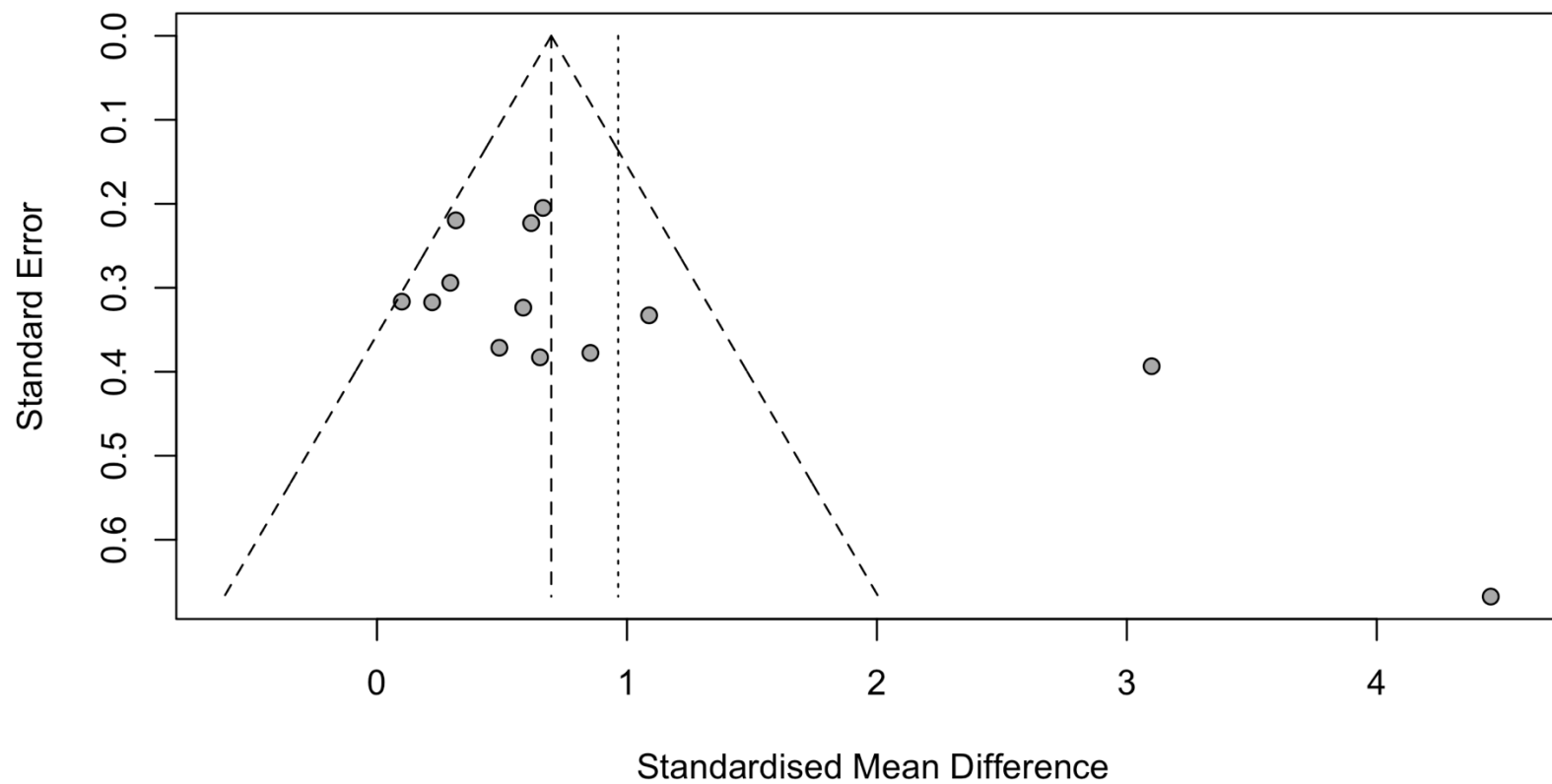
Supplementary Table 3. Split between direct and indirect evidence of different wavelengths of LLLT for knee pain.

Arm 1	Arm 2	k	I^2	Direct estimate [#]	Indirect estimate [#]	Network meta-analysis [#]	Incoherence
L1	L2	0	.	.	-0.61 [-1.92; 0.70]	-0.61 [-1.92; 0.70]	.
L1	MWL	1	.	-0.64 [-2.46; 1.17]	0.29 [-1.01; 1.60]	-0.02 [-1.08; 1.04]	0.41
L1	Sham	7	88.8%	0.84 [0.13; 1.55]	-0.25 [-4.03; 3.54]	0.81 [0.11; 1.50]	0.58
L2	MWL	0	.	.	0.59 [-0.83; 2.01]	0.59 [-0.83; 2.01]	.
L2	Sham	3	95.0%	1.42 [0.31; 2.53]	.	1.42 [0.31; 2.53]	.
MWL	Sham	4	34.2%	0.74 [-0.18; 1.65]	2.24 [-1.27; 5.75]	0.83 [-0.06; 1.72]	0.42

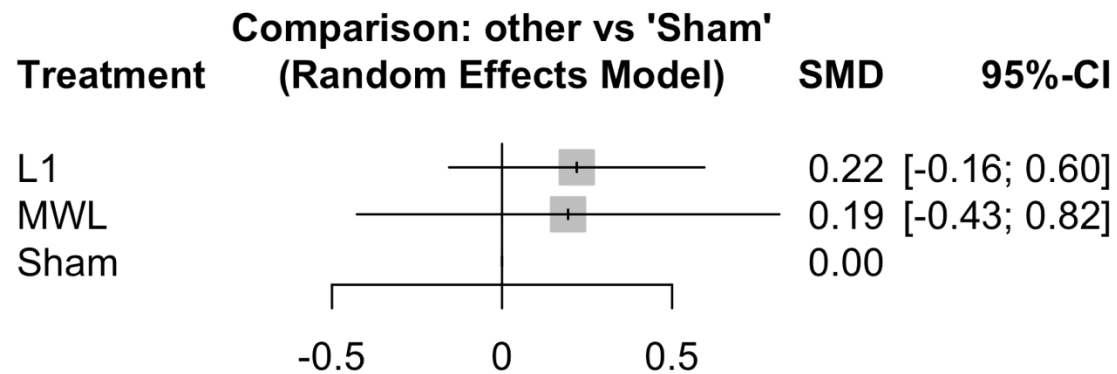
[#]Data are shown as standardized mean difference (SMD) and 95% credible intervals.

LLLT: low-level light therapy; L1: 785-850 nm LLLT; L2: 904-905 nm LLLT; MWL: multi-wavelength LLLT; Sham: sham LLLT;

Bolds are statistically significant.

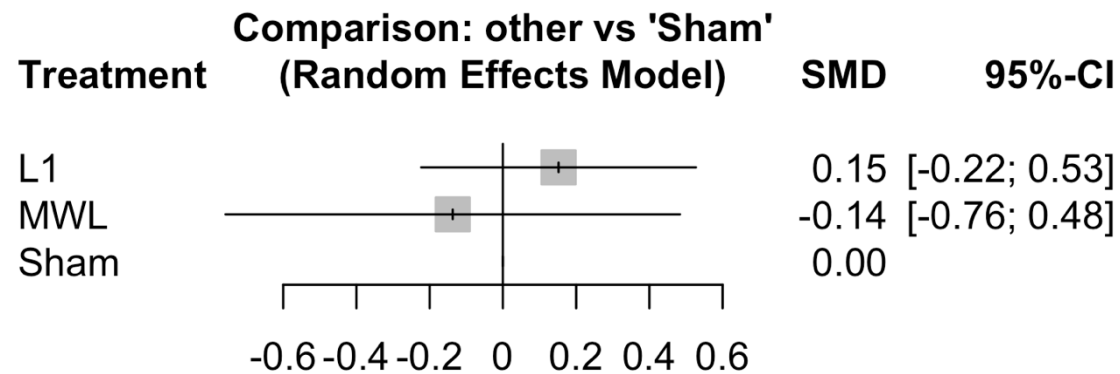


Supplementary Figure 1. Funnel plot representing publication bias for low-level light therapy on knee pain.



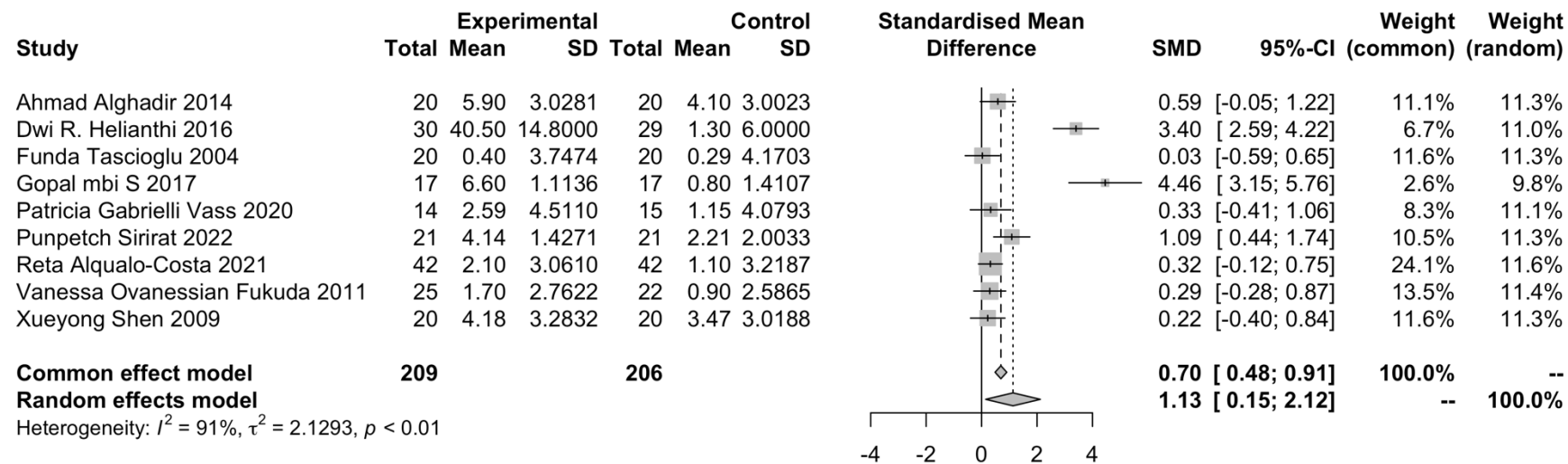
Supplementary Figure 2. Forest plot of network meta-analysis of different wavelength of LLLT for knee function.

LLLT: low-level light therapy; L1: 785-850 nm LLLT; MWL: multi-wavelength LLLT; Sham: sham LLLT; SMD: standardized mean difference



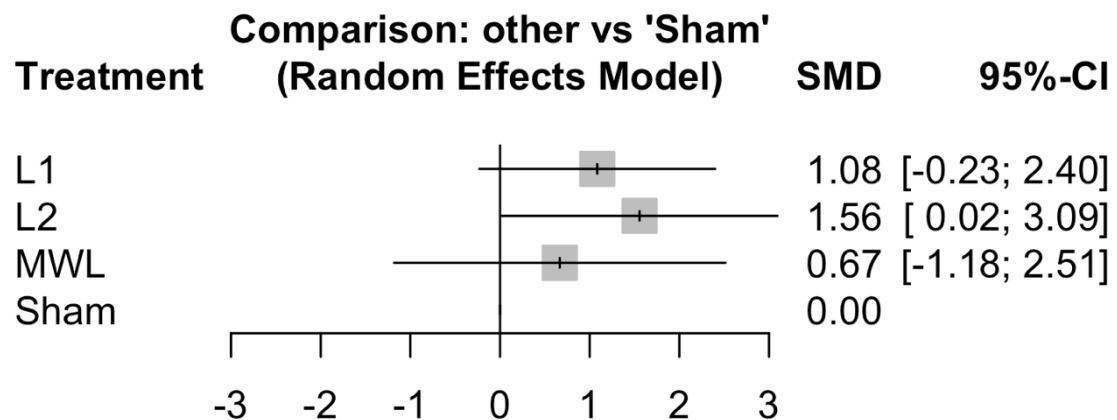
Supplementary Figure 3. Forest plot of network meta-analysis of different wavelength of LLLT for knee stiffness.

LLLTT: low-level light therapy; L1: 785-850 nm LLLT; MWL: multi-wavelength LLLT; Sham: sham LLLT; SMD: standardized mean difference



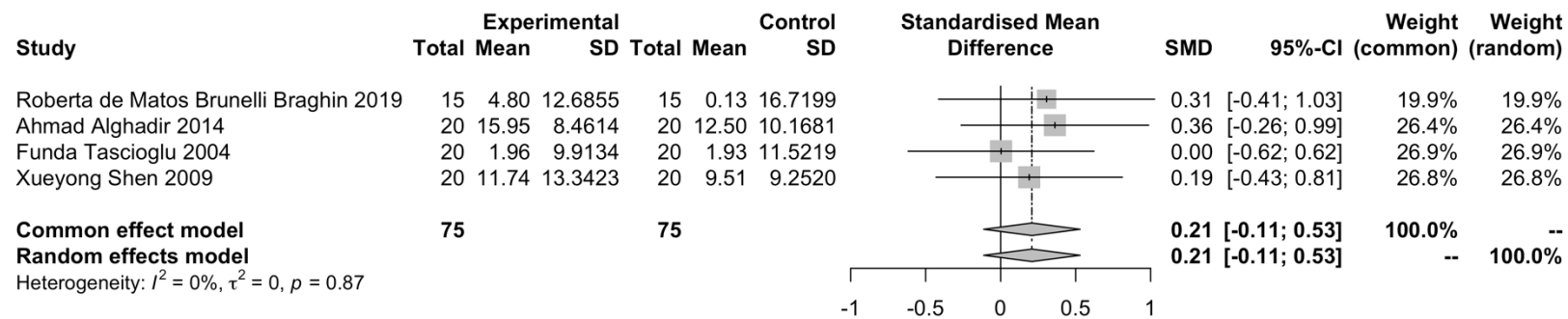
Supplementary Figure 4. Forest plot of direct evidence from direct comparisons for LLLT on knee pain after excluding high risk studies.

LLLT: low-level light therapy; SMD: standardized mean difference; SD: standard division



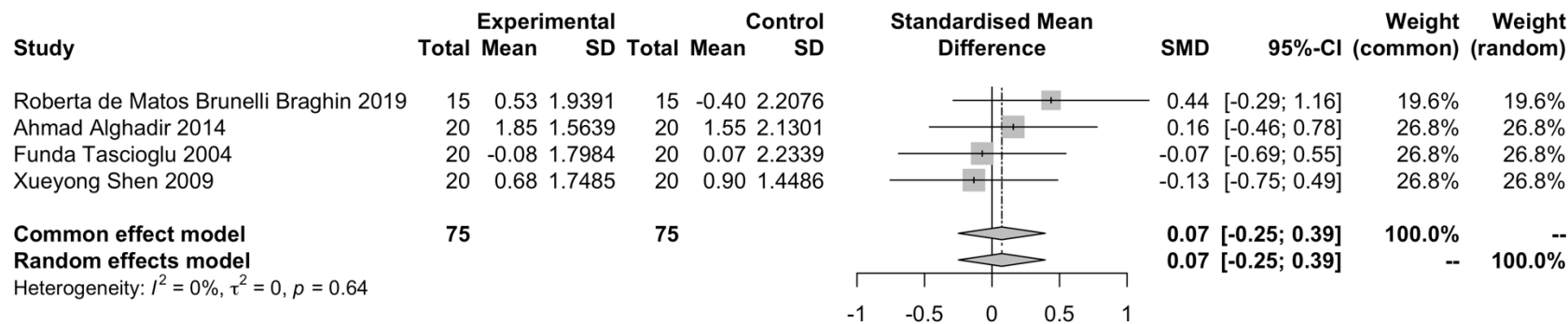
Supplementary Figure 5. A forest plot of network meta-analysis of different wavelengths of LLLT for knee pain after excluding high risk studies.

LLLT: low-level light therapy; L1: 785-850 nm LLLT; L2: 904-905 nm LLLT; MWL: multi-wavelength LLLT; Sham: sham LLLT; SMD: standardized mean difference



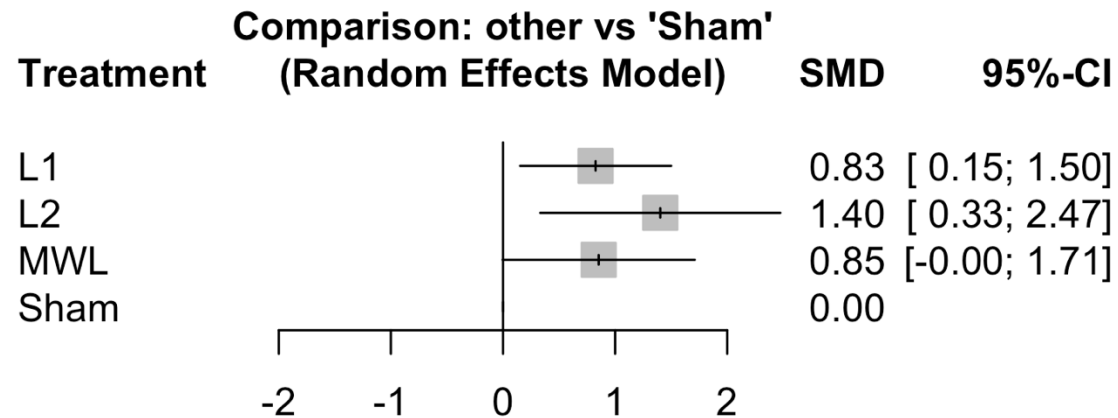
Supplementary Figure 6. Forest plot of direct evidence from direct comparisons for knee function.

SMD: standardized mean difference; SD: standard division



Supplementary Figure 7. Forest plot of direct evidence from direct comparisons for LLLT on knee stiffness.

LLLT: low-level light therapy; SMD: standardized mean difference; SD: standard division



Supplementary Figure 8. Forest plot of network meta-analysis of different wavelength of LLLT for knee pain.

LLLT: low-level light therapy; L1: 785-850 nm LLLT; L2: 904-905 nm LLLT; MWL: multi-wavelength LLLT; Sham: sham LLLT; SMD: standardized mean difference