



## EFFECT OF COLD AND HEAT THERAPIES ON PAIN RELIEF IN PATIENTS WITH DELAYED ONSET MUSCLE SORENESS: A NETWORK META-ANALYSIS

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**Objective:** To comprehensively compare the effectiveness of cold and heat therapies for delayed onset muscle soreness using network meta-analysis.

**Methods:** Eight Chinese and English databases were searched from date of establishment of the database to 31 May 2021. Cochrane risk-of-bias tool was used to analyse the included randomized controlled trials. Potential papers were screened for eligibility, and data were extracted by 2 independent researchers.

**Results:** A total of 59 studies involving 1,367 patients were eligible for this study. Ten interventions were examined: contrast water therapy, phase change material, the novel modality of cryotherapy, cold-water immersion, hot/warm-water immersion, cold pack, hot pack, ice massage, ultrasound, and passive recovery. Network meta-analysis results showed that: (i) within 24 h after exercise, hot pack was the most effective for pain relief, followed by contrast water therapy; (ii) within 48 h, the ranking was hot pack, followed by the novel modality of cryotherapy; and (iii) over 48 h post-exercise, the effect of the novel modality of cryotherapy ranked first.

**Conclusion:** Due to the limited quality of the included studies, further well-designed research is needed to draw firm conclusions about the effectiveness of cold and heat therapies for delayed onset muscle soreness.

**Key words:** network meta-analysis; cold therapy; heat therapy; delayed onset muscle soreness.

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Delayed onset muscle soreness (DOMS) is the sensation of pain and discomfort in the muscles, often after taking part in unaccustomed physical activity or high-force muscle work, which normally increases in intensity in the first 24–48 h after exercise and peaks at 24–72 h, then lessens, resolving by 5–7 days post-exercise (1). DOMS is a common myogenic condition, probably due to pathophysiological changes within the tissue resulting from micro-injuries (2). Although most

### LAY ABSTRACT

The effects of different methods of cold and heat therapy on pain in patients with delayed onset muscle soreness are debated, and there is uncertainty regarding the most effective of these therapies. The aim of this study was to evaluate the effects of different cold and heat treatments on pain in patients with delayed onset muscle soreness. Using network meta-analysis and ranking, it was found that, within 48 h post-exercise, use of hot-pack was superior to other interventions, whereas, over 48 h post-exercise, cryotherapy was the optimal intervention for pain relief in patients with delayed onset muscle soreness.

people will experience DOMS at some time, many accept that it is a self-limiting entity, and most do not seek medical or physiotherapeutic intervention. However, Lightfoot et al. (3) state that DOMS can be detrimental to exercise adherence and may have a drastic effect on performance. The symptoms can range from muscle tenderness to severe debilitating pain, which can reduce patients' performance (a reduction in joint range of motion, peak torque, mobility and flexibility, etc.) or seriously affect quality of life (1, 4).

Although the mechanisms and treatment strategies remain uncertain, various mechanisms that contribute to DOMS have been adopted, such as muscle spasm, lactic acid accumulation, injury to the muscles and connective tissues. The main bases supporting this theory (muscle connective tissue damage) are as follows: lower oxygen consumption and energy consumption during exercise, but more serious injuries and soreness, and damage to muscle fibres can be seen under the microscope. In addition to serum myoglobin, phosphokinase, trimethylhistidine and hydroxyproline are increased after exercise (5). According to the inflammatory response theory, DOMS is considered to be a series of inflammatory reactions caused by mechanical injury, and Ca<sup>2+</sup> plays a triggering role in the process of muscle soreness. Some inflammatory mediators are needed to produce pain in patients with DOMS, and prostaglandins are the most important inflammatory mediators. The increased concentration of leucolysin and Ca<sup>2+</sup> after exercise can stimulate

the synthesis of local prostaglandins (5). Therefore, according to these theoretical mechanisms, various treatments for DOMS are available, including non-steroidal anti-inflammatory drugs (NSAIDs), heat and cold therapy, stretching, transcutaneous electrical nerve stimulation (TENS), rest, etc. These therapies help to promote the recovery of muscle function, decrease the inflammatory response and alleviate the symptoms of DOMS (6, 7). It is worth noting that, among these, heat and cold therapy have become very popular, as they are low-cost and simple techniques that can be performed easily in different situations and can be applied by non-medical personnel (e.g. sports and fitness coaches). In addition, previous studies have reported the effectiveness of cold and heat therapy in reducing pain in patients with DOMS.

Cold therapies include cold-water immersion (CWI), cold pack, ice massage, the novel modality of cryotherapy (CRYO) and phase change material (PCM). The immersion temperature of CWI is usually  $\leq 15^{\circ}\text{C}$ ; CRYO is a treatment involving very short exposures to extreme cold dry air to the whole patient or to a treatment area (8, 9). The intervention forms of CRYO include whole- and partial-body cryotherapy and air-pulsed cryotherapy, with the temperature of the cryotherapy chamber at  $-30^{\circ}\text{C}$ ,  $-80$  to  $-110^{\circ}\text{C}$ , or  $< -110^{\circ}\text{C}$ ; the cold treatment temperature of PCM is  $15^{\circ}\text{C}$  (10). Cold treatment is thought to reduce swelling and cell metabolism, so that oedema, pain and injury are minimized (11).

Commonly used methods of heat therapy include hot/warm water immersion (HWI/WWI), hot pack, sauna and ultrasound. Heat treatment increases metabolism in tissues, promotes blood circulation and reduces pain (11). Another type of intervention is contrast water therapy (CWT), which is a combination therapy using cold and heat. The temperature range of cold therapy is generally less than or equal to  $10^{\circ}\text{C}$ ; and the temperature of the heat therapy  $35$ – $40^{\circ}\text{C}$ .

The effect of different methods of cold and heat therapy on pain in patients with DOMS is currently debated, and few studies have directly compared the effects of different cold and heat therapies; thus, the most effective cold and heat therapy for DOMS is unknown. Among them, there are many outcome variables for observing the effect of cold or heat therapy on DOMS, including subjective pain and objective indicators, such as creatine kinase (CK) and C-reactive protein (CRP), which are all important outcome observation indicators, and are independent of each other (12). However, in previous studies, reports of objective variables are inconsistent, but there are relatively numerous reports on the variable pain. Therefore, this study chose to conduct a network meta-analysis (NMA) on pain.

Using the same type of research object, an NMA can systematically compare several different types of intervention measures for a certain problem, and rank them according to the effect of a certain outcome index, to determine the best intervention scheme. NMA is used to evaluate the effectiveness of pain relief on different cold and heat methods in patients with DOMS, and to provide a basis for the clinical selection of appropriate cold and heat methods.

## METHODS

The protocols followed were based on the preferred reporting item of the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) statement (13). This study also followed our protocol, registered in PROSPERO (ID CRD42020170632).

### Search strategy

Searches were performed in the following databases: PubMed, CINAHL, the Cochrane Library, Web of Science and 4 Chinese databases (China National Knowledge Infrastructure (CNKI), VIP Database, Chinese Biomedical Database (CBM) and Wanfang Database), in order to conduct a comprehensive database retrieval, from the date of establishment of the database to 31 May 2021.

The following search keywords were used: “delayed onset muscle soreness”, “DOMS”, “muscle pain”, “myalgia”, “muscle soreness”, “muscular pain”, “muscular soreness”, “sore muscle”, “muscle tenderness”, “muscle ache”, “cryotherapy”, “ice”, “cool”, “cold”, “cold therapy”, “psychrotherapy”, “frigo-therapy”, “cold temperature”, “cold pack”, “phase change material”, “whole/partial-body cryotherapy”, “ice massage”, “heat”, “heating”, “heat therapy”, “heat treatment”, “hot”, “warm”, “thermal therapy”, “thermotherapy”, “hyperthermia therapy”, “induced hyperthermia”, “hot temperature”, “heat pack”, “ultrasound”, “spa”, “sauna”, “shower”, “steam”, “steam bath”, “contrast water therapy”, “hydrotherapy”, “contrast therapy”, “water immersion”, “heating and cooling combination therapy”, “whirlpool bath\*?”. The search terms used in PubMed are shown as an example in Table I. An additional manual search of references included in the study was performed, in order to find other articles that may have been overlooked.

### Inclusion criteria

The selection criteria used in this review were based on methodological and clinical factors, such as population, intervention, control, outcomes, and study design (PICOS) (13) criteria, as described below.

**Participants.** The patients included in the published articles were over 18 years of age, with DOMS after exercise. Inclusion of patients with DOMS was not restricted according to race, sex, nationality or profession.

**Intervention.** Studies needed to have participants receiving cold and heat therapy within 1 h after exercise (studies that repeated the intervention protocol on subsequent days were included). The treatment group intervention included cold, heat, or contrast water therapy (CWI, PCM, CWT, HWI/WWI, CRYO, cold pack, ice massage, hot pack, or ultrasound).

**Table I.** Keywords used in the PubMed database

Search	Query
#1	myalgia [Mesh]
#2	("delayed onset muscle soreness" OR DOMS OR "muscle pain" OR myalgia OR "muscle soreness" OR "muscular pain" OR "muscular soreness" OR "sore muscle" OR "muscle tenderness" OR "muscle ache") [Title/Abstract]
#3	#1 OR #2
#4	cryotherapy [Mesh]
#5	"cold temperature"[Mesh]
#6	(cryotherapy OR ice OR cool OR cold OR cold therapy OR psychrotherapy OR frigotherapy OR cold temperature OR cold pack OR ice massage OR phase change material OR whole/partial-body cryotherapy) [Title/Abstract]
#7	#4 OR #5 OR #6
#8	heating [Mesh]
#9	"hyperthermia, induced"[Mesh]
#10	"hot temperature"[Mesh]
#11	(heat OR heating OR heat therapy OR heat treatment OR hot OR warm OR thermal therapy OR thermotherapy OR hyperthermia therapy OR induced hyperthermia OR hot temperature OR heat pack OR ultrasound OR spa OR sauna OR shower OR steam OR steam bath) [Title/Abstract]
#12	#8 OR #9 OR #10 OR #11
#13	hydrotherapy [Mesh]
#14	(contrast water therapy OR hydrotherapy OR contrast therapy OR water immersion OR "heating and cooling combination therapy" OR whirlpool bath*) [Title/Abstract]
#15	#13 OR #14
#16	#7 OR #12 OR #15
#17	randomized controlled trial [Publication Type] OR randomized [Title/Abstract] OR placebo [Title/Abstract]
#18	#3 AND #16 AND #17

**Comparisons.** The control group interventions were passive recovery (PAS), including rest, no intervention or placebo.

**Outcome.** The outcome of DOMS was reported. Pain (muscle soreness) was measured on a visual analogue scale (VAS) pain score, Graphic Pain Rating Scale (GPRS), Likert scale, or modified Talag scale. Outcome variables were measured at baseline (pre-exercise) and post-exercise (24 h, 48 h, and over 48 h follow-up time).

Study design. Randomized controlled trials (RCTs) were selected.

#### Exclusion criteria

Studies were excluded if: (i) they were published in a language other than Chinese or English; (ii) re-published studies; (iii) there were insufficient data to report an effect size; (iv) they used multiple recovery modalities, including cold and heat treatment in conjunction with another recovery modality; or (v) participants had cardiovascular disease, hepatic disease, diabetes, obesity, etc.

#### Study selection and data extraction

The identified studies were selected by 2 authors independently. Titles and abstracts were scanned initially, and then the full articles were examined according to the inclusion criteria. In the case of disagreement, a third reviewer was consulted in order to reach a final consensus. Whenever clarification was needed, the paper's author was contacted for more information. Two reviewers independently extracted data from the included studies using standardized data extraction forms. For each study, data on the general characteristics of the study, research methods, participants, interventions, outcome measures, results, and other information were extracted.

#### Risk of bias assessment

Two reviewers independently assessed the risk of bias of included studies. According to the Cochrane Handbook for Systematic Reviews of Interventions (version 5.1.0) (14), this

assessment tool covers 7 domains, including random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other bias. Risk of bias for each field was scored low, high, or unclear. Any disagreement between the 2 authors was resolved by consensus and discussion with a third reviewer. Publication bias was assessed using a funnel plot.

#### Data synthesis and analysis

All studies underwent multiple follow-up (pre- and post-exercise) observations for each outcome, and the mean difference of the pain score post-exercise (24 h, 48 h and over 48 h follow-up time) from baseline (pre-exercise) change was calculated. Standardized mean difference (SMD) (different metrics are used across studies) and 95% confidence interval (95% CI) were used to assess the effects of different interventions on DOMS. Network meta-analysis compares multiple treatments simultaneously by combining direct and indirect evidence of the relative treatment effects. Stata software (version 16.0; StataCorp LLC, College Station, TX 77845, USA) was used to perform the network meta-analysis. The inconsistency factor (IF) was used to estimate the inconsistency in each closed loop. If there was a closed loop in the network (for example, A-B-C), then each comparison in the loop (for example, A-B) may be the result of an indirect comparison (for example, A-C and C-B). Therefore, the results of direct and indirect comparisons may be different. The lower limit of 95% CI of the inconsistency factor (IF) is close to 0, suggesting that the closed loop maintains consistency, with the consistency model selected for analysis. In the case of inconsistency, the inconsistency model was selected, and regression analysis or sensitivity analysis was used. Potential therapeutic benefits of interventions were ranked using surface area under the cumulative ranking curve (SUCRA) and MeanRank (15). The highest SUCRA score was 100%. Higher SUCRA scores, smaller corresponding MeanRank values, and higher rankings indicate better efficacy. Publication bias was evaluated using a funnel plot.

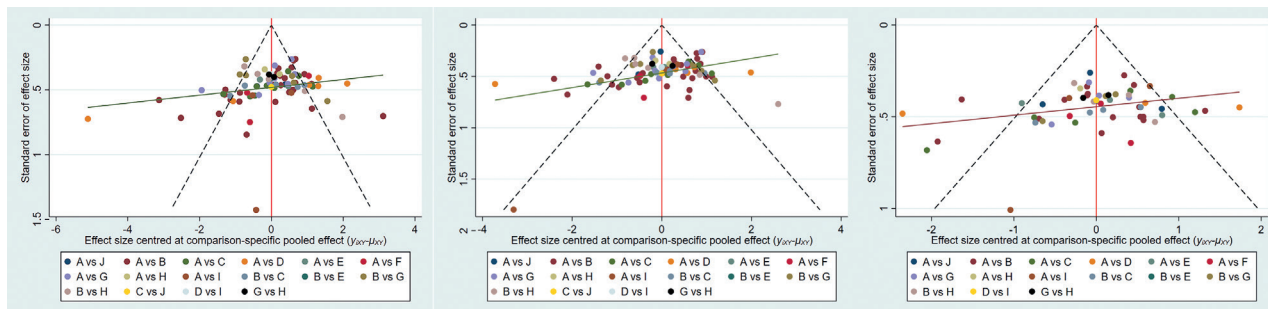




**Table II.** Characteristics of the included studies

Reference	Country	Number of cases (T/C)	Sex (male/female)	Profession	Mean age, years		Interventions*	
					T	C	T	C
Abaidia et al. 2017 (66)	FR/UK/AUS	10/10	10/0	Athletes	23.40±4.00		CWI	WBC
Adamczyk et al. 2016 (65)	PL/AUS	12/12	36/0	Non-athletes	22.50±0.90	22.10±0.70	Ice massage	PAS
		12/12		Non-athletes	22.50±0.80		CWI	
Ascensao et al. 2011 (64)	PT	10/10	20/0	Athletes	18.10±1.80	18.30±0.80	CWI	HWI
Aytar et al. 2008 (63)	TR	30/30	0/90	Non-athletes	22.00±2.08	21.60±2.14	Ultrasound	PAS
Bailey et al. 2007 (62)	UK	10/10	20/0	Non-athletes	23.60±4.10	21.70±2.00	CWI	PAS
Barber et al. 2020 (68)	UK	8/8	16/0	Athletes	20.00±1.20		CWI	PAS
Bruckner et al. 2005 (59)	AUS	20/20	11/29	Non-athletes	21.40±4.30	21.00±3.10	CWI	WWI
Behringer et al. 2018 (61)	DE	11/8	21/9	Athletes	26.10±3.00	24.00±1.70	Cold pack	PAS
Bouzdil et al. 2018 (60)	TN	8/8	8/0	Athletes	19.63±0.74		CWI	WWI
Ciccione et al. 1991 (58)	USA	10/10	0/40	Non-athletes	-	-	ultrasound	PAS
Clifford et al. 2018 (57)	UK/USA	11/11	11/0	Athletes	19.00±1.00		PCM	PAS
Costello et al. 2012 (9)	IE	9/9	-	Non-athletes	21.20±2.10		CRYO	PAS
Crystal et al. 2013 (56)	USA	10/10	20/0	Non-athletes	20.90±0.90	21.50±3.20	CWI	PAS
Crowther et al. 2017 (36)	AUS	29/29	29/0	Non-athletes	27.00±6.00		CWI	PAS
		29/29		Non-athletes			CWT	
Dantas et al. 2019 (55)	BR	10/10	20/0	Non-athletes	30.28±6.10	33.00±4.84	CWI	PAS
de Freitas et al. 2019 (54)	BR	6/6	12/0	Athletes	25.70±6.10	24.80±4.70	CWI	PAS
de Paiva et al. 2016 (53)	BR/USA	10/10	50/0	Non-athletes	-	-	Cold pack	PAS
Doeringer et al. 2018 (52)	USA	12/10	7/15	Athletes	-	-	CWI	PAS
Doungkula et al. 2018 (51)	TH/UK	16/16	32/0	Non-athletes	21.31±1.03		CRYO	PAS
Dantas et al. 2020 (70)	BR	10/10	20/0	Non-athletes	30.00±6.09	31.00±4.80	CWI	PAS
Elias et al. 2013 (49)	AUS	8/8	24/0	Athletes	19.90±2.80		CWI	PAS
		8/8		Athletes			CWT	
Elias et al. 2012 (50)	AUS	14/14	14/0	Athletes	20.90±3.30		CWI	PAS
		14/14		Athletes			CWT	
Eston et al. 1999 (48)	UK	8/7	0/15	Non-athletes	22.00±2.00		CWI	PAS
Ferreira-Junior et al. 2015 (47)	BR/USA	13/13	26/0	Non-athletes	20.20±2.70	20.30±2.20	CRYO	PAS
Fonda et al. 2013 (46)	SI	11/11	11/0	Non-athletes	26.90±3.80		CRYO	PAS
Fonseca et al. 2016 (45)	BR	4/4	8/0	Athletes	24.00±3.60		CWI	PAS
French et al. 2006 (44)	UK	10/6	26/0	Athletes	23.90±4.90	21.50±2.00	CWT	PAS
Glasgow et al. 2014 (43)	UK	20/10	32/18	Non-athletes	18–35		CWI	PAS
Guilhem et al. 2013 (8)	FR/AUS	12/12	24/0	Non-athletes	25.20±1.10	23.90±1.40	CRYO	PAS
Hauswirth et al. 2011 (67)	FR	9/9	-	Athletes	31.80±6.50		CRYO	PAS
		9/9	-	Athletes			Ultrasound	
Higgins et al. 2013 (42)	AUS	8/8	24/0	Athletes	19.50±0.80		CWI	PAS
		8/8		Athletes			CWT	
Hohenauer et al. 2020 (41)	CH/BE/UK	9/7	0/28	Non-athletes	21.90±2.00	23.30±2.60	CWI	PAS
		9/7		Non-athletes	22.40±3.00		CRYO	
Hohenauer et al. 2018 (40)	CH/BE/UK	9/10	19/0	Non-athletes	26.00±4.30	25.80±4.50	CWI	PBC
Howatson et al. 2005 (39)	UK	12/12	12/0	Non-athletes	24.80±5.30		Ice massage	PAS
Howatson et al. 2003 (38)	UK	9/9	9/0	Athletes	23.30±3.00		Ice massage	PAS
Ingram et al. 2009 (37)	AUS	11/11	11/0	Athletes	27.50±6.00		CWT	PAS
		11/11		Athletes			CWI	
Jakeman et al. 2009 (35)	UK	9/9	0/18	Athletes	19.90±0.97		CWI	PAS
Kositsky et al. 2020 (69)	FI	5/5	10/0	Athletes	19.40±0.90	18.4±0.50	CWI	PAS
Kuligowski et al. 1998 (34)	USA	14/14	28/28	Non-athletes	-	-	WWI	PAS
		14/14		Non-athletes			CWI	
		14/14		Non-athletes			CWT	
		14/14		Non-athletes			PCM	
Kwiecien et al. 2018 (33)	USA/UK/ZA	4/8	6/2	Non-athletes	37.00±12.00		PCM	PAS
Kwiecien et al. 2020 (32)	USA/UK/ZA	13/13	26/0	Athletes	25.00±6.00		PCM	PAS
Leeder et al. 2015 (31)	UK/ZA	8/8	24/0	Athletes	22.00±3.00	22.00±3.00	CWI	PAS
Lindsay et al. 2017 (30)	USA/NZ	7/8	15/0	Athletes	28.30±5.70		CWI	PAS
Machado et al. 2017 (29)	BR	40/20	60/0	-	21.00±2.25	20.40±1.80	CWI	PAS
Malmir et al. 2017 (7)	IR	16/10	-	Amateur athletes	26.00±3.00	26.00±3.00	Cold pack	PAS
Naugle et al. 2017 (28)	USA	12/13	4/45	Non-athletes	20.00±1.90		Cold pack	PAS
Petrofsky et al. 2017 (27)	USA/KOR	20/20	-	Non-athletes	26.00±2.60	25.30±3.00	Hot pack	PAS
Petrofsky et al. 2015 (11)	USA	20/20	-	Non-athletes	25.50±2.70	25.30±3.00	Cold pack	PAS
		20/20		Non-athletes	26.10±2.60		Hot pack	
Petrofsky et al. 2012 (26)	USA	5/5	8/12	Athletes	25.80±3.10	26.50±13.30	Hot pack	PAS
Pointon et al. 2011 (25)	AUS	10/10	10/0	Athletes	21.00±1.60		Cold pack	PAS
Sellwood et al. 2007 (24)	AUS	20/20	11/29	Non-athletes	21.40±4.30	21.00±3.10	CWI	WWI
Siqueira et al. 2018 (23)	BR	15/15	30/0	Non-athletes	20.50±1.40	19.90±1.40	CWI	PAS
Skurvydas et al. 2006 (22)	LT	20/20	20/0	Non-athletes	20.40±1.70		CWI	PAS
Vaile 2008 et al. (21)	AUS/NZ	12/38	38/0	Non-athletes	-	-	CWI	PAS
		11/38		Non-athletes	-	-	HWI	
		15/38		Non-athletes	-	-	CWT	
Vaile 2007 et al. (20)	AUS/NZ/UK	13/13	4/9	Non-athletes	26.20±5.80	26.20±5.80	CWT	PAS
Vieira 2016 et al. (19)	BR/AUS	28/14	42/0	Non-athletes	21.15±2.50	20.20±1.70	CWI	PAS
Wilson 2017 et al. (18)	UK	11/10	31/0	Non-athletes	41.30±7.60	40.60±7.20	CWI	PAS
		10/10		Non-athletes	37.70±8.90		CRYO	
Wilson 2019 et al. (17)	UK	8/8	24/0	Non-athletes	21.88±3.40	25.88±5.19	CWI	PAS
		8/8		Non-athletes	26.50±8.40		CRYO	
Yanagisawa 2003 et al. (16)	JP	9/10	28/0	Non-athletes	23.80±1.80		CWI	PAS

AUS: Australia; BE: Belgium; BR: Brazil; CA: Canada; CH: Switzerland; DE: Germany; FI: Finland; FR: France; IE: Ireland; IR: Iran; JP: Japan; KOR: South Korea; LT: Lithuania; LU: Luxembourg; NZ: New Zealand; PL: Poland; PT: Portugal; SI: Slovakia; TN: Tunisia; TR: Turkey; TH: Thailand; ZA: South Africa; -: not mentioned. \*All studies applied the intervention measures within 1 h after exercise. PAS: (Passive recovery: rest, no intervention or placebo). CWI (cold water immersion; CRYO (the novel modality of cryotherapy; PCM (phase change material; CWT (contrast water therapy); and HWI/WWI (hot/warm water immersion).



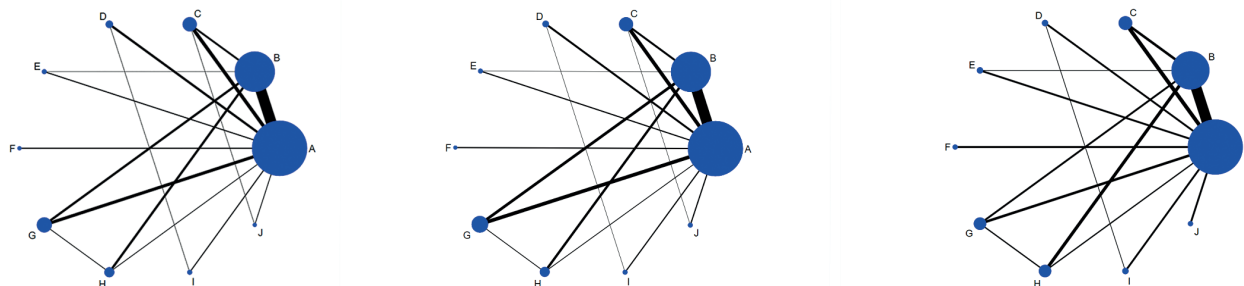
**Fig. 3.** Funnel plot of the efficacy of 7 interventions of cold and heat therapies and one passive recovery (control group). Left: 24 h; middle: 48 h; right: >48 h. A: passive recovery (PAS); B: cold water immersion (CWI); C: the novel modality of cryotherapy (CRYO); D: cold pack, E: ice massage, F: phase change material (PCM); G: contrast water therapy (CWT); H: hot/warm water immersion (HWI/WWI); I: hot pack, J: ultrasound.

and heat therapy interventions and 1 passive recovery were compared. A total of 10 interventions were included in the network meta-analysis: CWI, CRYO, PCM, CWT, HWI/WWI, cold pack, hot pack, ice massage, ultrasound and PAS (7–9, 11, 16–70). The use of hot pack within 1 h after exercise resulted in the best pain relief within 48 h post-exercise. Use of CRYO within 1 h after exercise has a significant effect on pain relief over 48 h post-exercise. At the 24 h follow-up after exercise, the 10 interventions were ranked as follows: hot pack, CWT, CRYO, PCM, cold pack, CWI, ice massage, ultrasound, HWI/WWI, PAS. At 48 h post-exercise, the ranking was: hot pack, CRYO, PCM, CWT, ultrasound, CWI, HWI/WWI, cold pack, ice massage, PAS. At over 48 h, the ranking of analgesic effect was: CRYO, PCM, CWT, hot pack, ice massage, CWI, cold pack, HWI/WWI, ultrasound, PAS.

Hot pack is one of the oldest interventions in cold and heat therapies. Compared with other interventions, the technology is safer and more mature. Hot pack can resist the loss of heat after exercise, keep tissue warm, increase blood flow speed and metabolism, and speed up clearance of inflammatory factors, thus reducing pain in patients (27). In the network meta-analysis, the results show that the effect of hot pack is ranked the first within 48 h. Several previous studies (4, 26, 71) have also found that thermal therapy is effective

in reducing acute, non-specific low back pain and pain in patients with DOMS. The reason may be the increasing skin temperature 24 h after exercise in all subjects, probably due to higher blood flow in muscle, inflammation, and repair of tissue damage caused by the exercise. Therefore, timely heat therapy after exercise can reduce the loss of muscle tissue temperature, maintain a constant temperature in the tissue, promote blood circulation to the affected area, increase the supply of nutrients and oxygen to the injured area, accelerate metabolism, and reduce peripheral nerve excitability, thereby alleviating pain. However, studies have shown that heat pack only changes the temperature of the subcutaneous tissue to a depth of 1–2 cm below the skin surface, suggesting that any temporary effects related to pain relief after intervention may soon wear off. Therefore, hot pack may only have a better effect on pain within 48 h after exercise. However, there were few studies of the application of hot pack for DOMS, and the difference between the temperature and form of hot pack may cause inconsistency in the study, affecting the stability of the results. Thus, the results should be treated with caution. More relevant clinical RCTs of hot packs are required in the future.

The analgesic effect of CRYO (the novel modality of cryotherapy) was gradually superior to other intervention measures, with an increase in rest time



**Fig. 4.** Network plot of 10 treatment methods. Left: within 24 h follow-up time; middle: within 48 h follow-up time; right: >48 h follow-up time. A: passive recovery (PAS); B: cold water immersion (CWI); C: the novel modality of cryotherapy (CRYO); D: cold pack, E: ice massage, F: phase change material (PCM); G: contrast water therapy (CWT); H: hot/warm water immersion (HWI/WWI); I: hot pack, J: ultrasound.

**Table III.** Follow-up time: 24 h–network meta-analysis of the different interventions to alleviate the pain of delayed-onset muscle soreness (DOMS) (standardized mean difference (SMD) (95% confidence interval; 95% CI)).

Ultrasound																				
4.41 (1.70,7.12)	Hot pack																			
-0.28 (-2.55to1.98)	-4.69 (-7.02to-2.37)	HWI/WWI																		
1.03 (-1.07to3.13)	-3.38 (-5.54to-1.22)	1.31 (-0.25to2.88)	CWT																	
0.91 (-1.28to3.11)	-3.50 (-5.75to-1.24)	1.20 (-0.50to2.89)	-0.12 (-1.58to1.34)	PCM																
0.17 (-2.45to2.79)	-4.24 (-6.91to-1.57)	0.45 (-1.76to2.67)	-0.86 (-2.91to1.19)	-0.74 (-2.89to1.40)	Ice massage															
0.51 (-1.55to2.57)	-3.90 (-6.02to-1.77)	0.80 (-0.72to2.31)	-0.52 (-1.77to0.73)	-0.40 (-1.81to1.01)	0.34 (-1.67to2.35)	Cold pack														
0.97 (-1.22to3.16)	-3.44 (-5.69to-1.19)	1.25 (-0.43to2.93)	-0.06 (-1.51to1.39)	0.06 (-1.53to1.64)	0.80 (-1.34to2.94)	0.46 (-0.94to1.85)	CRYO													
0.25 (-1.68to2.19)	-4.16 (-6.16to-2.15)	0.54 (-0.80to1.88)	-0.78 (-1.81to0.25)	-0.66 (-1.88to0.56)	0.08 (-1.80to1.96)	-0.26 (-1.22to0.70)	-0.72 (-1.92to0.49)	CWI												
-1.19 (-2.31to-0.08)	1.01 (-0.78to2.80)	0.43 (-1.76to2.63)	0.51 (-0.88to1.90)	-0.48 (-0.93to-0.02)	0.36 (-0.98to1.70)	-1.52 (-2.59to-0.45)	0.18 (-1.70to2.06)	-0.11 (-1.30to1.09)	PAS											

**Table IV.** Follow-up time: 48 h network meta-analysis of the different interventions to alleviate the pain of DOMS (SMD (95%CI)).

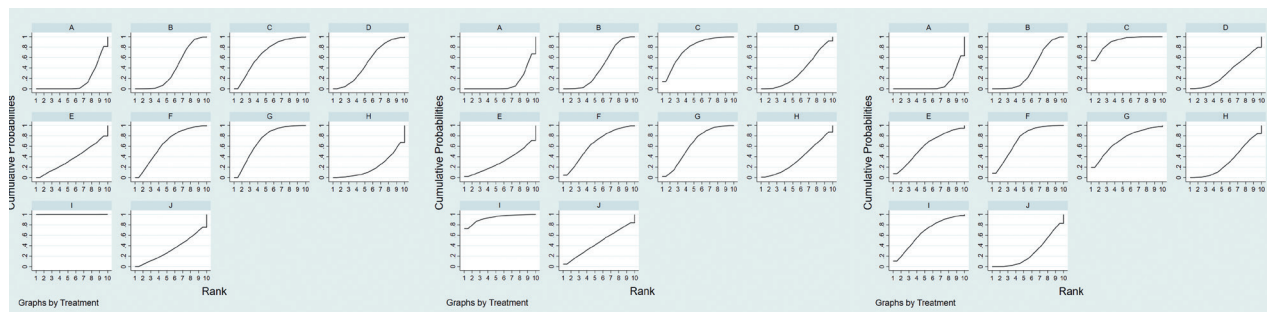
Ultrasound																				
1.68 (-0.68to4.05)	Hot pack																			
-0.17 (-2.23to1.89)	-1.85 (-3.83to0.13)	HWI/WWI																		
0.40 (-1.48to2.27)	-1.29 (-3.08to0.51)	0.57 (-0.79to1.93)	CWT																	
0.47 (-1.53to2.47)	-1.21 (-3.13to0.71)	0.64 (-0.88to2.17)	0.08 (-1.20to1.35)	PCM																
-0.32 (-2.70to2.06)	-2.01 (-4.32to0.31)	-0.15 (-2.15to1.85)	-0.72 (-2.53to1.09)	-0.80 (-2.73to1.14)	Ice massage															
-0.19 (-2.10to1.72)	-1.87 (-3.70to-0.04)	-0.02 (-1.43to1.39)	-0.59 (-1.72to0.54)	-0.66 (-1.99to0.66)	0.13 (-1.72to1.98)	Cold pack														
0.77 (-1.23to2.77)	-0.91 (-2.83to1.01)	0.95 (-0.58to2.47)	0.38 (-0.90to1.65)	0.30 (-1.15to1.75)	1.10 (-0.84to3.04)	0.96 (-0.36to2.29)	CRYO													
-0.01 (-1.78to1.76)	-1.69 (-3.37to-0.01)	0.16 (-1.05to1.38)	-0.40 (-1.27to0.46)	-0.48 (-1.59to0.63)	0.31 (-1.39to2.02)	0.18 (-0.76to1.13)	-0.78 (-1.89to0.33)	CWI												
-1.40 (-2.42to-0.37)	1.02 (-0.62to2.66)	0.58 (-1.43to2.58)	0.66 (-0.61to1.94)	-0.61 (-1.04to-0.18)	0.43 (-0.78to1.64)	-0.70 (-1.59to0.19)	-0.02 (-1.73to1.69)	-0.29 (-1.40to0.81)	PAS											

**Table V.** Follow-up time: over 48 h network meta-analysis of the different interventions to alleviate the pain of DOMS (SMD (95%CI))

Ultrasound																				
0.83 (-0.59to2.25)	Hot pack																			
0.11 (-1.04to1.26)	-0.72 (-2.22to0.79)	HWI/WWI																		
1.04 (-0.62to2.69)	0.21 (-1.71to2.12)	0.93 (-0.80to2.65)	CWT																	
0.93 (-0.18to2.04)	0.10 (-1.37to1.58)	0.82 (-0.39to2.03)	-0.11 (-1.80to1.59)	PCM																
0.70 (-0.81to2.22)	-0.13 (-1.93to1.67)	0.59 (-1.00to2.18)	-0.33 (-2.32to1.65)	-0.23 (-1.79to1.34)	Ice massage															
0.07 (-1.12to1.27)	-0.75 (-2.30to0.79)	-0.03 (-1.33to1.26)	-0.96 (-2.72to0.79)	-0.85 (-2.11to0.41)	-0.63 (-2.25to1.00)	Cold pack														
1.55 (0.23to2.88)	0.72 (-0.92to2.37)	1.44 (0.03to2.86)	0.52 (-1.33to2.36)	0.62 (-0.76to2.01)	0.85 (-0.87to2.58)	1.48 (0.02to2.93)	CRYO													
0.19 (-0.65to1.03)	-0.64 (-1.92to0.64)	0.08 (-0.89to1.05)	-0.85 (-2.38to0.69)	-0.74 (-1.66to0.18)	-0.51 (-1.90to0.87)	0.11 (-0.91to1.14)	-1.36 (-2.54to-0.19)	CWI												
-3.50 (-5.19to-1.81)	-1.81 (-2.92to-0.71)	1.29 (-0.23to2.81)	1.42 (0.13to2.71)	-0.45 (-0.85to-0.05)	-0.21 (-1.17to0.76)	0.12 (-1.37to1.60)	-0.09 (-1.46to1.28)	-0.60 (-1.74to0.53)	PAS											

PAS: passive recovery; CWI: cold water immersion; CRYO: the novel modality of cryotherapy; PCM: phase change material; CWT: contrast water therapy; HWI/WWI: hot/warm water immersion). Statistically significant findings are in bold: when the 95% CI did not contain "0", pairwise comparison of interventions is statistically significant, i.e.,  $p$ -value < 0.05; when the 95% CI contained 0, pairwise comparison of interventions is not statistically significant, i.e.,  $p$ -value  $\geq$  0.05). SMD < 0 indicates that the intervention in the column is more effective than the intervention in the line in reducing the level of pain; SMD > 0 indicates that the intervention in the line is more effective than the intervention in the column in reducing the level of pain.





**Fig. 5.** Surface area under the cumulative ranking curve (SUCRA) of A: passive recovery (PAS); B: cold water immersion (CWI); C: the novel modality of cryotherapy (CRYO); D: cold pack; E: ice massage; F: phase change material (PCM); G: contrast water therapy (CWT); H: hot/warm water immersion (HWI/WWI); I: hot pack and J: ultrasound) treatment for the pain of patients with delayed onset muscle soreness (DOMS). Left: 24 h follow-up time; middle: 48 h follow-up time; right: > 48 h follow-up time.

after exercise. At a follow-up point of more than 48 h post-exercise, CRYO ranks first and shows the best analgesic effect. As a new cryotherapy, CRYO is similar to other traditional cold therapies. That is, by reducing muscle, skin and core temperature to stimulate cutaneous receptors and sympathetic adrenergic fibres, local blood vessels constrict, reducing local tissue metabolism and inflammation, and reducing the sensitivity of receptors and nerve conduction velocity, thus relieving the pain of patients with DOMS (72, 73). The pattern of intervention in CRYO involves exposure to extremely cold dry air (< -100°C) in an environmentally controlled room for short periods of time, and patients are exposed to vaporized liquid nitrogen in a head-free cabin (41), or localized application of very cold air (-30°C) on the skin and the subepidermal tissues by convection (8). Considering the extremely low temperature, the researchers only allowed patients to undergo CRYO for 2–5 min. However, this technique was found to be advantageous. A short period of application could reduce the intensity of pain and promote the recovery of DOMS through exposure to extremely cold air. Our results showed that CRYO was less effective than hot pack and CWT for analgesia within 48-h post-exercise, which may be because extremely low

temperature stimulation did not provide a comfortable temperature for the patients when they received the cold therapy intervention. However, after the patients received cold therapy (more than 48 h post-exercise), the hypothermic effect of CRYO still affected the skin tissue, and the analgesic effect was gradually significant. CRYO may be a double-edged sword, as adverse reactions may occur due to its extremely low temperature. Although Banfi et al. (74) concluded that the new cryotherapy is safe and does not have a deleterious effect on immunological or cardiac function, there was some evidence that it is beneficial for muscle pain and harmful for the recovery of muscle function in a randomized controlled trial (RCT) (18). Therefore, future research should enhance the monitoring and reporting of adverse reactions, in order to improve the safety and effectiveness of the CRYO interventions.

Both PCM and CRYO belong to new type of cold therapy with the same mechanism of action. Our results showed that at the follow-up point of more than 48 h post-exercise, the cumulative area under the curve of PCM was the second largest value, indicating that the analgesic effect of PCM was second only to that of CRYO and superior to other interventions. analgesic effect on DOMS. PCM can prolong the duration of cryotherapy exposure while allowing the patient to continue with activities of daily living, which are absent from other interventions (75). PCM could not only maintain its own constant temperature, but also maintain the patient’s skin temperature at 22°C during 3 h of application (57). One study (76) reported that PCM helped untrained individuals to recover from muscle injury and is more effective at alleviating the severity of pain in patients with DOMS. Although PCM has a good analgesic effect on patients with DOMS in our study, there were only 3 relevant studies, the number of studies and the sample size are small, and the first author of 2 studies is the same. In addition, the experimental design of the included original studies is limited. This may produce a placebo effect when participants receive PCM intervention, especially for

**Table VI.** Ranking according to efficacy outcomes of surface under the cumulative ranking curve (SUCRA)

Intervention	24 h		48 h		> 48 h	
	SUCRA%	Mean rank	SUCRA%	Mean rank	SUCRA%	Mean rank
PAS	15.1	8.6	11.2	9.0	9.8	9.1
CWI	38.7	6.5	42.5	6.2	38.4	6.5
CRYO	67.3	3.9	76.8	3.1	90.3	1.9
Cold pack	51.1	5.4	34.1	6.9	32.3	7.1
Ice massage	37.0	6.7	31.2	7.2	60.0	4.6
PCM	65.3	4.1	64.7	4.2	72.9	3.4
CWT	71.5	3.6	64.4	4.2	71.3	3.6
HWI/WWI	20.6	8.1	36.5	6.7	32.2	7.1
Hot pack	99.9	1.0	93.1	1.6	65.6	4.1
Ultrasound	33.4	7.0	45.5	5.9	27.2	7.6

SUCRA: surface under the cumulative ranking curve. PAS: passive recovery; CWI: cold water immersion; CRYO: the novel modality of cryotherapy; PCM: phase change material; CWT: contrast water therapy; HWI/WWI: hot/warm water immersion.



subjective pain measurement. Therefore, more high-quality studies are needed to confirm the analgesic effect of PCM.

At the 24-h post-exercise follow-up point, CWT ranked second only to hot pack in analgesic effect. In the included studies, CWT intervention time was relatively long (mean 14 min). The mean water temperature of cold immersion in CWT was 12°C, and that of hot immersion was between 38°C and 42°C. CWT relieves pain in DOMS patients by producing hydrostatic pressure (77). And, the hydrostatic pressure is not related to the water temperature, but is related to the depth of immersion. In addition to the mechanisms of hydrotherapy, cold or heat therapy has a unique advantage. Benefits associated with CWT may be linked to changes in intra-muscular hydrostatic pressure by alternating vasoconstriction and vasodilation, which may alter blood flow in immersed musculature (78). CWT is associated with an increase in limb blood flow during warm immersion and a decrease during cold immersion (78). The alternate vasodilatation and vasoconstriction of the peripheral blood vessels has been proposed to increase lactate clearance, decrease oedema and increase blood flow (20, 79). These effects may play a positive role in relieving pain in patients with DOMS. However, at the follow-up point 24 h later, according to the area probability ranking under the curve, the analgesic effect of CWT decreases slightly, indicating that the effect is not sustained for a long time and the pain of DOMS may be relieved only temporarily. However, compared with the 2 new cold therapy methods (PCM and CRYO), the use of CWT may be relatively simple and safe. However, it should be noted that the intervention time and temperature of CWT in each study included were not completely the same, and the exercise training program for inducing DOMS has not been unified so far, so these factors may affect the accuracy of our results.

In summary, hot pack is better at reducing pain in patients with DOMS within 48 h follow-up times. CRYO is a primary choice for pain relief over 48 h post-exercise, and PCM is a suboptimal choice. This study showed that these latter 2 treatments may be good choices. However, hot pack is superior to CRYO and PCM with regard to safety and convenience. However, there are few reports on the application of the method in patients with DOMS. CRYO and PCM may have side-effects, so it is important to closely observe and monitor the changes in patients' vital signs and functions when applying this technology. Taking these factors into account, CWT may be considered a priority to alleviate the pain response caused by DOMS.

However, it is important to note that these recommendations should be treated with caution. The patient's sex, different exercise protocols, therapy

intervention (time, temperature, frequency, etc.), and other factors may affect the stability of the results of this study. To date, there is no unified standard and regulation for the therapy intervention (time, frequency, temperature, etc.) of cold and heat therapy. Jinnah et al. (10) recommend use of cold pack for more than 10 min to relieve the pain of DOMS. For CWI, Jinnah et al. believe that soaking in cold water at 11–15°C for 11–15 min is the most appropriate. In the included studies, most of the CWI intervention times were 10–15 min, and the mean intervention temperature was 10–15°C. This result seems to be consistent with previous research. In the included studies, the intervention time for cold pack was usually 20 min. For the hot pack, 3 studies applied low-intensity hot pack for 8 h, while the other study applied the hot pack for 30 min. It is difficult to draw a clear conclusion on the differences in the intervention time. However, according to the characteristics of the included studies, we suggest that it is more appropriate to soak for 10–15 min in cold water at 10–15°C for the application of CWI, while, for hot pack, a longer intervention is recommended. However, one point needs to be made clear; when choosing any kind of intervention, it is important to fully evaluate the patient's physical condition, in order to select appropriate and effective intervention measures, and avoid the occurrence of frostbite or scald and other risks. Regarding sex, most of the included studies had only female, or only male, subjects. Therefore, sex may have influenced the results of the study. Hohenauer (12) conducted a subgroup analysis of the sexes, and found that men are more likely than women to benefit from cooling. According to Petrofsky (11), the thickness of fat in the area where DOMS occurs may be a factor influencing the effectiveness of heat or cold therapy. The thicker the subcutaneous fat, the slower the process of heat and cold therapy. However, fat thickness is not measured or analysed in any of the included studies. Therefore, whether sex differences and adipose tissue influence the intervention effect of heat or cold therapy requires further research, with more female participants. Regarding the change in intensity of the exercise programme, schemes for exercise-induced muscle injury vary from long sprints to competition. Subgroup analysis according to different exercise regimens was considered, but was not possible due to the wide range of exercise regimens included in the study. Therefore, future research is needed to determine a standard training programme to induce DOMS, in order to ensure stability of the results.

#### *Strengths and limitations*

This study has several strengths. The fundamental strength of the current analysis is the use of robust

methodology. The comprehensive literature search was performed in 8 electronic databases, with an exhaustive search of articles and complementary sources. Secondly, to the best of our knowledge, this is the first network meta-analysis comparing the efficacy of different cold and heat therapies. The strengths of this systematic review relate mainly to the study interventions, which aim to rank the effectiveness of existing heat and cold therapy in reducing the pain of DOMS. However, this network meta-analysis has several limitations. First, the quality of the included studies varied. Some studies were better designed RCTs with adequate randomization; however, most studies had weak blinding/allocation. In trials with subjectively assessed outcomes, lack of adequate allocation, concealment, or blinding, tend to produce over-optimistic estimates of the effects of interventions (80). However, the pain score that needs to be analysed in this study belongs to the subjective evaluation result; thus, a lack of blinding would be expected to introduce bias if knowledge of the intervention groups affected the care received or the assessment of outcomes. Therefore, researchers should improve the transparency of the trial, and perform sufficient randomized allocation and complete blinding. Due the real-life situation, a relevant trial study of hot and cold therapy cannot achieve complete blinding, but a placebo control group could be included to avoid overstating the effects of an intervention. Secondly, in the included studies, the number of studies including some interventions was limited and the sample size was small, which may have affected the stability of the results resulting in publication bias and small sample size study effects. Finally, both publication and language restriction bias may have influenced the results.

### Conclusion

This meta-analysis compared the effectiveness of 9 cold and heat modalities and 1 passive recovery (PAS) on pain relief on patients with DOMS. Regarding the 2 follow-up effectiveness time-points (within 48 h), hot pack proved more effective and stable for pain relief compared with other interventions and is therefore a promising candidate for clinical application. If only the effectiveness of the intervention is considered, CRYO is a primary choice for pain relief over 48 h after exercise in our study, and PCM is a suboptimal choice. For professional athletes and any other subjects with DOMS, PCM and CRYO are helpful. But their side-effects and adverse reactions on the body have been less reported. Therefore, compared with CRYO and PCM, the use of CWT may be relatively simple and safe. In addition, due to the large inconsistencies in relevant studies on cold and hot pack included in this analysis, the effect of hot pack on reducing the degree

of pain due to DOMS should be studied further in more detail. Further research and more high-quality RCTs are required to draw firm conclusions.

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