

# Whole-body cryotherapy: empirical evidence and theoretical perspectives

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**Abstract:** Whole-body cryotherapy (WBC) involves short exposures to air temperatures below  $-100^{\circ}\text{C}$ . WBC is increasingly accessible to athletes, and is purported to enhance recovery after exercise and facilitate rehabilitation postinjury. Our objective was to review the efficacy and effectiveness of WBC using empirical evidence from controlled trials. We found ten relevant reports; the majority were based on small numbers of active athletes aged less than 35 years. Although WBC produces a large temperature gradient for tissue cooling, the relatively poor thermal conductivity of air prevents significant subcutaneous and core body cooling. There is weak evidence from controlled studies that WBC enhances antioxidant capacity and parasympathetic reactivation, and alters inflammatory pathways relevant to sports recovery. A series of small randomized studies found WBC offers improvements in subjective recovery and muscle soreness following metabolic or mechanical overload, but little benefit towards functional recovery. There is evidence from one study only that WBC may assist rehabilitation for adhesive capsulitis of the shoulder. There were no adverse events associated with WBC; however, studies did not seem to undertake active surveillance of predefined adverse events. Until further research is available, athletes should remain cognizant that less expensive modes of cryotherapy, such as local ice-pack application or cold-water immersion, offer comparable physiological and clinical effects to WBC.

**Keywords:** whole-body cryotherapy, cooling, recovery, muscle damage, sport

## Introduction

Cryotherapy is defined as body cooling for therapeutic purposes. In sports and exercise medicine, cryotherapy has traditionally been applied using ice packs or cold-water immersion (CWI) baths. Recently, whole-body cryotherapy (WBC) has become a popular mode of cryotherapy. This involves exposure to extremely cold dry air (usually between  $-100^{\circ}\text{C}$  and  $-140^{\circ}\text{C}$ ) in an environmentally controlled room for short periods of time (typically between 2 and 5 minutes). During these exposures, individuals wear minimal clothing, gloves, a woolen headband covering the ears, a nose and mouth mask, and dry shoes and socks to reduce the risk of cold-related injury. Although it was originally developed to treat chronic medical conditions, such as multiple sclerosis and rheumatoid arthritis,<sup>1</sup> WBC is being increasingly employed by athletes. Its purported effects include decreased tissue temperature, reduction in inflammation, analgesia, and enhanced recovery following exercise. WBC is typically initiated within the early stages (within 0–24 hours) after exercise and may be repeated several times in the same day or multiple times over a number of weeks.

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WBC is becoming increasingly accessible for athletes. It is considerably more expensive than traditional forms of cryotherapy, but it is not clear whether it offers any additional clinical effect. A recent review by Banfi et al<sup>2</sup> found observational evidence that WBC modifies many important biochemical and physiological parameters in human athletes. These include a decrease in proinflammatory cytokines, adaptive changes in antioxidant status, and positive effects on muscular enzymes associated with muscle damage (creatine kinase and lactate dehydrogenase). They also concluded that exposure to WBC is safe and does not deleteriously effect cardiac or immunological function. However, when this review<sup>2</sup> was published, few randomized trials examining the efficacy of the treatment had been completed. Further, the conclusions were predominantly based on lower-quality observational studies, which did not include a control group and therefore should be treated with caution.

A common supposition is that the extreme nature of WBC offers significant advantages over traditional methods of cooling, such as CWI or ice-pack application. Recently, there has been a large increase in the volume of research investigating the effects of WBC. Our aim is to update the evidence base, with a particular focus on reviewing empirical evidence derived from controlled studies. The objectives were: 1) to quantify the tissue-temperature reductions associated with WBC and compare these with traditional forms of cryotherapy; 2) to examine the biochemical and physiological effects of WBC exposure compared to a control, and to determine any associated adverse effects; and 3) to consider the strength of the clinical evidence base supporting its use in sports recovery and soft-tissue injury management.

## Materials and methods

A literature search was undertaken using Medline, Embase, and the Cochrane Controlled Trials Register up to October 2013. For our first objective, we sourced any studies quantifying temperature reductions associated with WBC. We extracted data (mean  $\pm$  standard deviation) on skin, intramuscular, and core-temperature reductions induced by WBC. No restrictions were made on the temperature-measurement device. For comparison, we used a convenience sample of studies reporting tissue-temperature reductions induced by ice-pack application (crushed ice) and CWI based on durations of 10 minutes and 5 minutes, respectively. These durations were selected as they align well with current clinical practice.<sup>3,4</sup>

For our second objective, we focused on studies fulfilling the following inclusion criteria: controlled studies comparing WBC intervention to a control group (observational studies

and studies using within-subject designs were excluded); the temperature of exposure had to have been at least  $-100^{\circ}\text{C}$ , though there were no restrictions placed on the number of exposures; participants could be healthy, or recovering from exercise or soft-tissue injury at the time of the intervention; no restrictions were made on participants' age, sex, or training status. We extracted all data relating to biochemical, physiological, or performance/clinical outcomes.

Key study characteristics were extracted by the primary researcher and tabulated. Outcomes were subgrouped into biochemical, perceived sensation, and performance-based measures. We were particularly interested in between-group differences based on follow-up scores. Where possible, effect sizes (standardized mean differences [MDs] and 95% confidence intervals [CIs]) were calculated from group means and standard deviations, using RevMan software (version 5.2; Nordic Cochrane Centre, Copenhagen, Denmark).

## Characteristics of controlled studies

Key study characteristics<sup>5–14</sup> are summarized in Table 1. Three studies<sup>8,10,13</sup> used randomized controlled designs, with all incorporating high-quality methods based on computer-generated randomization, allocation concealment, and blinded outcome assessment. The remainder of the studies<sup>5–7,9,11,12,14</sup> used controlled or crossover designs, with washout periods varying between 3<sup>7</sup> and 16 weeks.<sup>5</sup>

The majority of studies were undertaken using young, active participants with mean ages under 35 years. Just under 40% of participants were females. Four studies recruited high-performance athletes.<sup>5–8</sup> In three studies,<sup>9,10,12</sup> the objective was simply to examine the effect of WBC compared to an untreated control intervention using a sample of healthy participants. Six studies<sup>5–8,10,11</sup> used WBC either in the early stages after exercise or intermittently throughout a particular training block. One study<sup>13</sup> investigated the clinical effectiveness of WBC using a sample of participants with adhesive capsulitis of the shoulder joint.

In all studies, the WBC intervention involved a brief exposure to an acclimatization chamber or prechamber before entering a therapy chamber at  $-110^{\circ}\text{C}$  to  $-195^{\circ}\text{C}$  for 2.5–3 minutes. The total number of treatment sessions varied between one session on a single day<sup>12</sup> up to 20–24 sessions over a period of weeks.<sup>5,13</sup>

## Results

### Tissue-temperature reductions

Table 2 shows the relative temperature reductions associated with typical applications of ice packs, CWI, and WBC.<sup>12,15–29</sup>

Table 1 Study characteristics

Study design	Participants	WBC (control)	Outcomes	Higher values in WBC (vs control)	Lower values in WBC (vs control)	No between-group differences
Mila-Kierzenkowska et al <sup>5</sup> Crossover study (4-month washout)	n=9 Olympic-level kayakers undertaking a 10-day training cycle (all female, mean age 23.9±3.2 years) Cointerventions Antioxidant supplementation	n=9 exposed to -120°C to -140°C for 3 minutes; 20 sessions in total: twice per day over a 10-day period (n=9 no WBC)	Catalase TBARS	Superoxide dismutase Glutathione peroxidase		
Hauswirth et al <sup>6</sup> Randomized crossover study (3-week washout)	n=9 well-trained runners undertaking a simulated 48-minute trail run (all male, mean age 31.8±6.5 years)	n=9 exposed to -110°C for 3 minutes; 3 sessions in total: immediately, 24, and 48 hours postexercise (n=9 seated rest)	Strength	Pain Tiredness	Creatine kinase	
Pournot et al <sup>7</sup> Randomized crossover study (3-week washout)	n=11 trained runners undertaking a simulated 48-minute trail run (all male, mean age 31.8±6.5 years)	n=11 exposed to -110°C for 3 minutes; 4 sessions in total: immediately, 24, 48, and 72 hours postexercise (n=11 seated rest)	IL-1ra	CRP	IL-1β IL-6 IL-10 TNFα Leukocyte count Creatine kinase Leukocyte count Cortisol Testosterone	
Ziemann et al <sup>8</sup> Randomized controlled trial	n=12 professional male tennis players undertaking moderate-intensity training for 5 days (all male, mean age 20±2 years control, 23±3 years WBC)	n=6 exposed to -120°C for 3 minutes; 10 sessions in total: twice per day over 5 days (n=6 no WBC)	IL-6 Tennis-stroke effectiveness	TNFα		
Miller et al <sup>9</sup> Controlled trial	n=94 healthy participants (46 male, 48 female, mean age 37.5±3.1 years WBC, 37.9±2.1 years control)	n=46 exposed to -130°C for 3 minutes; 10 sessions in total: 1 session per day over 10 days (n=48 no WBC)	Total antioxidant status Superoxide dismutase Uric acid TBARS			
Costello et al <sup>10</sup> Randomized controlled trial	n=36 healthy participants (24 male, 12 female, mean age 20.8±1.2 years)	n=16 exposed to -110°C for 3 minutes; 2 sessions in a single day, 2 hours apart (n=16 exposed to 15°C)		Joint positional sense <sup>a</sup> MVIC		
Costello et al <sup>10</sup> Randomized controlled trial	n=18 participants (4 female, 14 male, mean age 21.2±2.1 years) undertaking 100 high-force maximal eccentric contractions of the left knee extensors	n=9 exposed to -110°C for 3 minutes; 2 sessions in a single day, 2 hours apart (n=9 exposed to 15°C)		MVIC Pain Peak power output		
Fonda and Sarabon <sup>11</sup> Randomized crossover (10-week washout)	n=11 participants (all male, mean age 26.9±3.8 years) undertaking high-load and eccentric lower-limb exercises	n=11 exposed to -140°C to -195°C for 3 minutes; 6 sessions in total: 1 per day over 6 days (n=11 no WBC)		Pain at rest Pain on squat	Creatine kinase Lactate dehydrogenase Aspartate aminotransferase Performance <sup>b</sup> Epinephrine Dopamine (PBC)	
Hauswirth et al <sup>12</sup> Controlled trial	n=40 healthy participants (all male; mean age 33.9±12.3 years control, 34.6±11.5 years WBC, 33.3±13.8 years PBC)	n=15 exposed to -110°C WBC for 3 minutes; n=15 exposed to -160°C PBC for 3 minutes; (n=10 seated rest)	Norepinephrine Dopamine (WBC) Heart-rate variability			

(Continued)

Table 1 (Continued)

Study design	Participants	WBC (control)	Outcomes		
			Higher values in WBC (vs control)	Lower values in WBC (vs control)	No between-group differences
Ma et al <sup>13</sup> Randomized controlled trial	n=30 participants with adhesive capsulitis of the shoulder joint (24 female, 6 male, mean age 57.2±6.6 years)	n=15 exposed to -110°C for 4 minutes; 24 sessions in total: 2 sessions per day, 3 times per week over 4 weeks plus standard physiotherapy treatment (n=15 standard physiotherapy treatment only)	ROM	Pain	
			Function		
Schall et al <sup>14</sup> Randomized crossover (1-week washout)	n=11 participants (all female, mean age 20.3±1.8 years) undertaking a 3-minute-maximum swimming exercise bout	n=9 exposed to -110°C for 3 minutes; 1 session immediately after exercise (n=9 30 minutes of passive recovery)	Indices of heart-rate variability	Performance (subjective judging in synchronized swimming)	
			Metabolic recovery (lactate VO <sub>2</sub> peak)		
			Subjective recovery		

**Notes:** <sup>a</sup>Absolute, relative, and variable error; <sup>b</sup>countermovement jump, power, strength.

**Abbreviations:** WBC, whole-body cryotherapy; vs, versus; TBARS, thiobarbituric acid reactive substances; IL, interleukin; ra, receptor antagonist; CRP, C-reactive protein; TNF, tumor necrosis factor; MVIC, maximum voluntary isometric contraction; PBC, partial body cryotherapy; ROM, range of movement.

Table 2 Tissue-temperature reductions by cooling modalities

	Ice pack (10 minutes)	CWI (4–5 minutes, 8°C–10°C)	WBC (3 minutes)
Skin temperature	18 <sup>b,15</sup>	6.2 (0.5) <sup>24</sup>	3.5–8.7 <sup>27</sup>
	20 <sup>a,16</sup>	8.4 (0.7) <sup>25</sup>	6.7 <sup>b,28</sup>
	20 <sup>b,17</sup>	9.0 (0.8) <sup>26</sup>	8.1 (0.4) <sup>c,12</sup>
	20 <sup>18</sup>		12.1 (1.0) <sup>25</sup>
	22 <sup>a,b,19</sup>		10.3 (0.6) <sup>26</sup>
Intramuscular temperature (2 cm depth)	25.7–26.4 <sup>20</sup>		13.7 (0.7) <sup>12</sup>
			19.4 <sup>b,29</sup>
	1.76 (1.37) <sup>21</sup>	1.7 (0.9) <sup>25</sup>	1.2 (0.7) <sup>25</sup>
	2.0 <sup>a,16</sup>		
	2.0 <sup>a,b,19</sup>		
Core temperature	2.7 <sup>b,15</sup>		
	–3.88 (1.83) <sup>22</sup>		
	0 <sup>a,16</sup>	0.2 (0.1) <sup>24</sup>	0 <sup>29</sup>
	0 <sup>23</sup>	0.4 (0.2) <sup>25</sup>	0.3 (0.2) <sup>25</sup>

**Notes:** <sup>a</sup>Data extracted from graphs with permission: Arch Phys Med Rehabil, 2001;82, Jutte LS, Merrick MA, Ingersoll CD, Edwards JE. The relationship between intramuscular temperature, skin temperature, and adipose thickness during cryotherapy and rewarming. 845–850.16 © 2001 with permission from Elsevier; and Merrick MA, Jutte LS, Smith ME. Cold modalities with different thermodynamic properties produce different surface and intramuscular temperatures. J Athl Train. 2003;38:28–33.19 <sup>b</sup>standard deviation not available. <sup>c</sup>PBC. All values are degrees celsius (means ± standard deviation).

**Abbreviations:** CWI, cold-water immersion; WBC, whole-body cryotherapy; PBC, partial body cryotherapy (head out).

The largest skin-temperature reductions seemed to be associated with ice-pack application. The skin-temperature reductions associated with CWI and WBC seemed to vary slightly across studies. Two studies<sup>25,26</sup> reported similar skin temperatures associated with a 4-minute WBC exposure at -110°C (thigh, 17.9°C±1.4°C; knee, 19.0°C±0.9°C) and a 4-minute CWI at 8°C (thigh, 21.3°C±1.2°C; knee, 20.5°C±0.6°C). Table 2 clearly highlights that subcutaneous tissue temperature reductions were consistently small regardless of the cooling medium. Intramuscular temperatures at 2 cm depth were rarely cooled below 2°C. Again, there were trends that ice packs induced slightly larger intramuscular temperature reductions in comparison to CWI and WBC. Core-temperature reductions were consistently small across all cooling modes.

## Inflammatory biomarkers

Pournot et al<sup>7</sup> compared a WBC intervention to a passive control after an intense simulated trail run using high-level athletes. Levels of inflammatory biomarkers (interleukin [IL]-1β, IL-1 receptor antagonist [ra], IL-6, IL-10, tumor necrosis factor [TNF]-α, and leukocytes) during the 4-day recovery period were generally similar in each group. The largest between-group differences were higher IL-1ra immediately after the first exposure, and lower concentration of C-reactive protein at 24, 48, 72, and 96 hours postexercise within the WBC condition. In a small study, Ziemann et al<sup>8</sup>

randomized professional tennis players to undertake twice-daily WBC or no intervention during a 5-day training camp. Two of the participants in this study could not be randomized due to contraindications to WBC and were therefore preselected for the control intervention. Their results showed an enhanced cytokine profile within the WBC group, with lower levels of TNF $\alpha$  and a higher concentration of IL-6.

## Muscle damage

There was evidence from three studies<sup>6,8,11</sup> that WBC does not affect markers of muscle damage after exercise. These studies found few differences between WBC and control groups in creatine kinase, lactate dehydrogenase, and aspartate aminotransferase during recovery from exercise-induced muscle damage (EIMD),<sup>11</sup> intense running,<sup>6</sup> or 5 days of moderate-intensity tennis training.<sup>8</sup>

## Oxidative stress

Miller et al<sup>9</sup> examined oxidative stress and antioxidant function using a group of nonexercising participants. The results showed an increase in antioxidant status associated with WBC in comparison to the untreated control group; however, there were only small between-group differences in relation to lipid peroxidation. As oxidative stress and antioxidant function were quantified at two different sites (ie, vascular and intracellular), it is difficult to conclude a strong relationship between WBC and free radical production. In a crossover study, Mila-Kierzenkowska et al<sup>5</sup> examined antioxidant status in Olympic kayakers undertaking training cycles both with and without WBC stimulation (twice per day). Results showed an attenuation of oxidative stress as measured by lipid peroxidation in the WBC group over the course of a 10-day training bout. This finding did not align with the majority of the athletes' enzymatic profiles (super-oxide dismutase and glutathione peroxidase), which were also surprisingly lower in the WBC condition in comparison to the exercise-only condition.

## Autonomic nervous system

Hausswirth et al<sup>12</sup> reported significant increases in nor-epinephrine concentrations in the immediate stages after cryostimulation compared to resting controls. They found similar between-group differences in resting vagal-related heart-rate variability indices (the root-mean-square difference of successive normal R-R intervals, and high-frequency band). An interesting caveat was that the magnitude of these effects was reduced when participants substituted WBC for a partial body cryostimulation that did not involve head

cooling. Another randomized study<sup>12</sup> examined the effects that WBC has on autonomic function, with a primary focus on parasympathetic reactivation after two maximal synchronized swimming bouts. Comparisons were made against active, passive, and contrast water-therapy conditions. The WBC condition (3 minutes at  $-110^{\circ}\text{C}$ ) had the largest influence on parasympathetic reactivation, with large increases across a range of similar heart-rate variability indices.

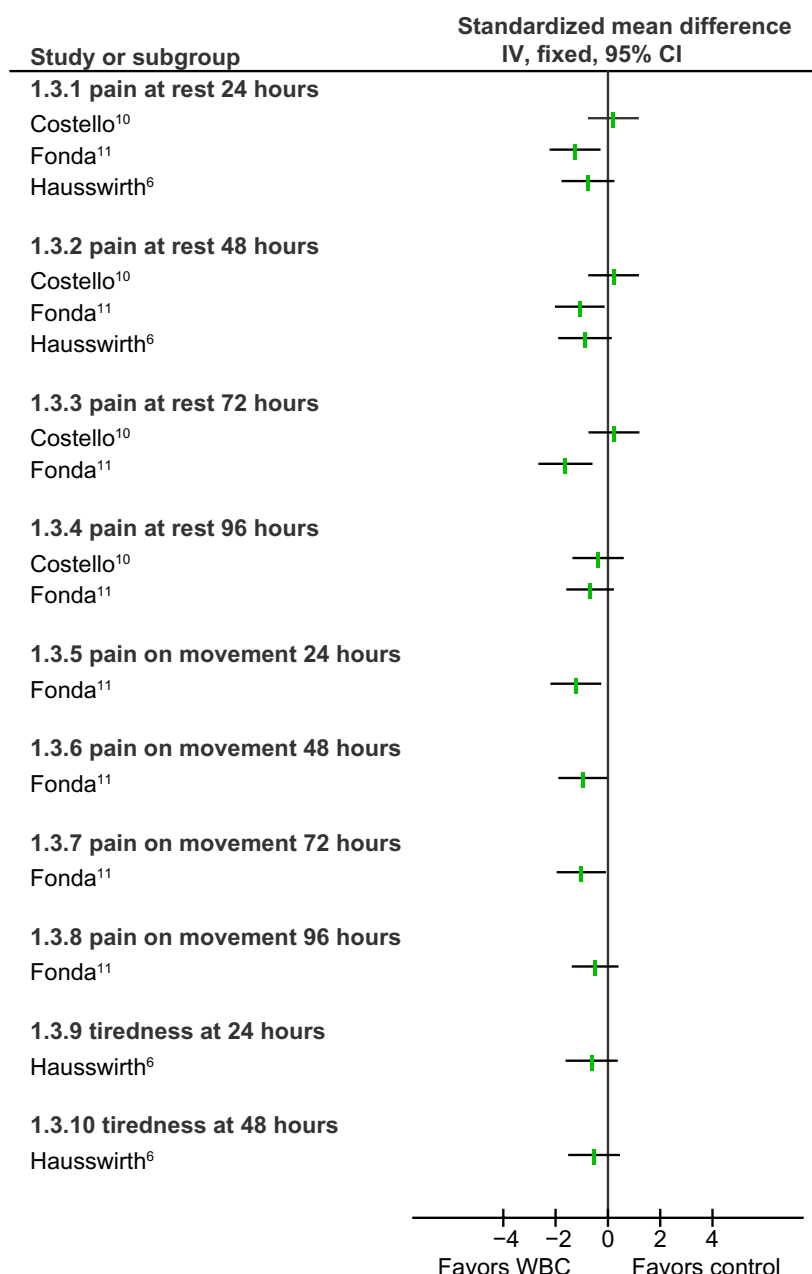
## Perceived and functional recovery

Using a randomized controlled design, Costello et al<sup>10</sup> found that 3-minute exposures at  $-110^{\circ}\text{C}$  had little effect on joint positional sense and muscle function compared to control exposures at  $15^{\circ}\text{C}$ . A follow-up study within the same report<sup>10</sup> examined the effectiveness of WBC compared to resting control using a subgroup of participants exposed to EIMD: results showed few differences between groups in terms of participants' strength, power, and muscle soreness. Fonda and Sarabon<sup>11</sup> also investigated the effects of WBC on functional recovery after EIMD, but incorporated a more intense cooling dose based on temperatures of  $-195^{\circ}\text{C}$ , using a liquid nitrogen system, and treatment up to 6 days postexercise. These investigators also found few significant differences between groups in relation to strength and power output; however, they reported significantly lower muscle soreness in favor of WBC. It is important to consider that Costello et al<sup>10</sup> incorporated a randomized controlled design, allocation concealment, and blinded outcome assessor, and was less open to selection and reporting bias.

Two studies investigated the effects of WBC on functional recovery after running- or sporting-based activities. Hausswirth et al<sup>6</sup> found that undertaking WBC immediately and at 24 and 48 hours after intense trail running resulted in significant improvements in strength, pain, and subjective fatigue compared to untreated controls. Ziemann et al<sup>8</sup> also recorded improved functional recovery associated with WBC within a group of elite tennis players. They found that athletes incorporating twice-daily exposure to  $-120^{\circ}\text{C}$  during a 5-day training camp had greater shot accuracy during two testing sessions, compared to an untreated control. These findings may be subject to detection bias, as blinded outcome assessors were not employed.

Schaal et al<sup>14</sup> found that compared to a passive control, a single WBC exposure (3 minutes at  $-110^{\circ}\text{C}$ ) enhanced subjective and metabolic recovery (based on blood lactate and  $\text{VO}_{2\text{max}}$ ) after intense bouts of swimming. This study found few differences when comparisons were made to an active recovery condition. Figures 1 and 2 provide a summary of the effects of WBC on perceived and functional recovery after exercise when compared to control intervention.





**Figure 1** Forest plot of perceived sensation.

**Abbreviations:** IV, inverse variance; CI, confidence interval; WBC, whole-body cryotherapy.

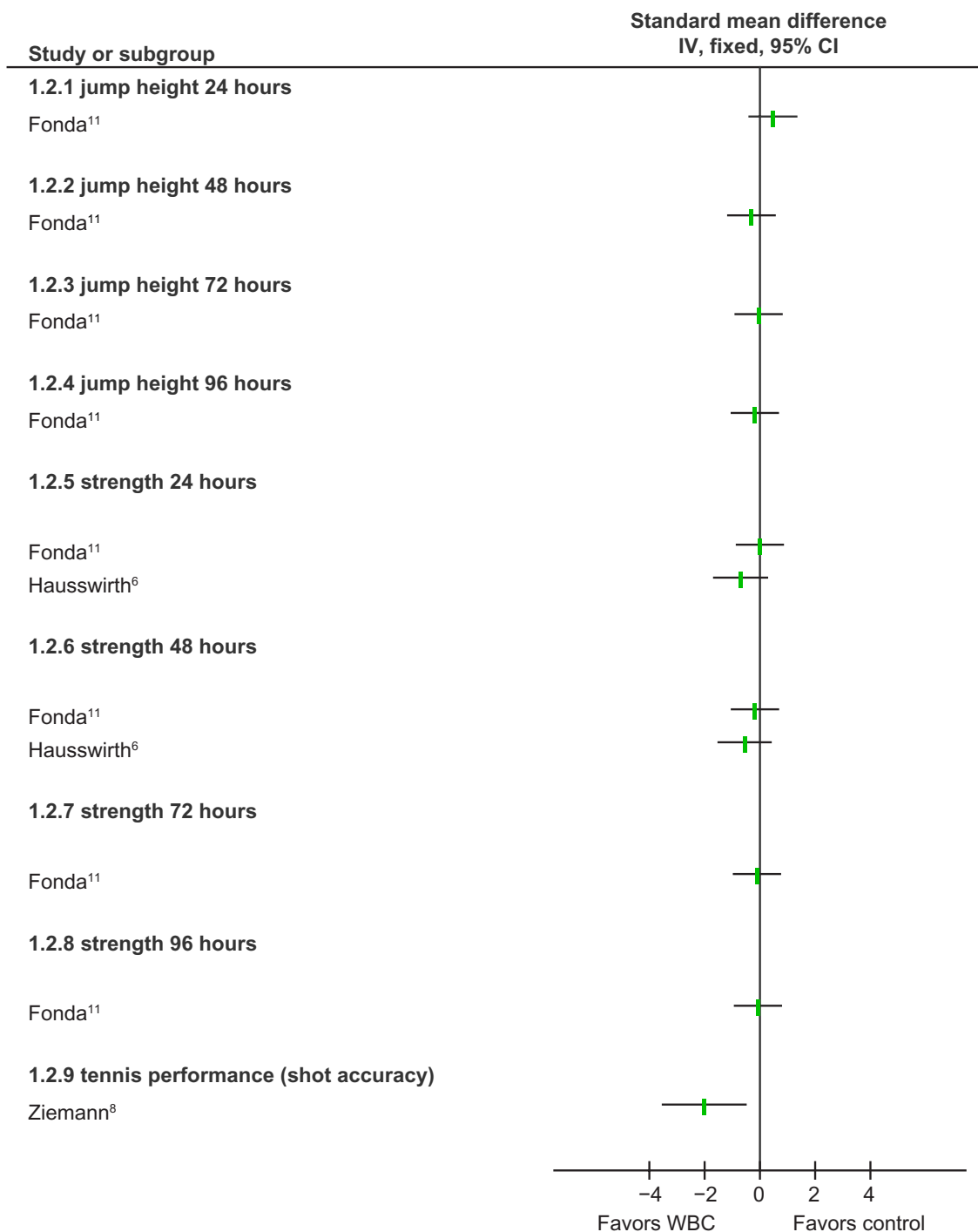
## Clinical outcomes

One study<sup>13</sup> examined the effectiveness of WBC on recovery from a musculoskeletal injury. Participants with adhesive capsulitis were randomized to receive either physiotherapy alone or physiotherapy in addition to WBC. After 4 weeks of treatment, both groups improved in terms of pain, shoulder function, and range of movement (ROM). Between-group comparisons were significantly in favor of WBC for all outcomes; in most cases, these were clinically meaningful with large mean differences in ROM (MD 13° abduction, 95% CI 9.2°–16.8°; MD 5° external

rotation, 95% CI 3.2°–6.7°), pain (MD, 1.2 cm, 95% CI 0.8–1.6, based on a 10 cm visual analog scale), and shoulder function (MD 4 points, 95% CI 3.1–4.9, based on a 30-point scale). Of note, this study<sup>13</sup> did not continue outcome assessment beyond the 4 weeks of treatment; therefore, any long-term effectiveness is unclear.

## Discussion

This review examined the biochemical, physiological, and clinical effects of WBC. We found that most of the research in



**Figure 2** Forest plot of performance outcomes.

**Abbreviations:** IV, inverse variance CI, confidence interval; WBC, whole-body cryotherapy.

this area has been undertaken using small groups of younger (predominantly male) participants. In over half of the studies, the primary objective was to determine mechanisms of effect associated with WBC based on biochemical markers. A small number of studies focused on perceived recovery and performance-based measurement after various sport and exercise exposures. Only one study investigated the clinical

effectiveness of WBC based on participants with significant musculoskeletal injury.

### Tissue-temperature reduction

The premise of cryotherapy is to extract heat from the body tissue to attain various clinical effects. To optimize these effects, the best evidence suggests that a critical level of tissue

cooling must be achieved.<sup>30,31</sup> As such, a key objective of this review was to determine the magnitude of tissue-temperature reductions associated with WBC and to compare with traditional forms of cooling (ice pack, CWI) used in sport and exercise medicine.

There is a supposition that because of its extreme temperatures ( $-110^{\circ}\text{C}$ ), WBC offers an enhanced cooling effect over traditional forms of cryotherapy. It is clear that exposure to  $-110^{\circ}\text{C}$  creates a large thermal gradient between the skin and the environment ( $\sim 140^{\circ}\text{C}$ ). However, heat transfer depends on a number of additional factors. For example, thermal conductivity or heat-transfer coefficient ( $k = \text{W}/\text{m}^2 - \text{K}$ ) is the ability of a material to transfer heat. Ice has a much higher heat-transfer coefficient (2.18 k) compared to both water (0.58 k) and air (0.024 k), meaning that it is a more efficient material for extracting heat energy from the body. Ice application also exploits phase change (change from solid into liquid), further enhancing its cooling potential. Although water and air are not the best media to transfer heat, a potential advantage is that they facilitate large surface areas of the body to be cooled simultaneously.

Comparisons across empirical studies suggest that the largest skin-temperature reductions are usually associated with crushed-ice application. Temperature reductions associated with CWI and WBC seem less intense, and in some reports these did not reach the critical temperatures necessary to optimize analgesia.<sup>30</sup> Of note, intramuscular temperature reductions seem to be negligible, regardless of the mode of cooling. To date, only one study<sup>25</sup> has examined the effect of WBC on intramuscular temperature, and future research addressing this gap in the literature is warranted.

The thermal properties of biological tissue mean that it is fundamentally difficult to cool below the skin surface. Subcutaneous adipose tissue has a very low thermal conductivity (0.23 k; by comparison, muscle has a value of 0.46 k),<sup>32</sup> causing it to have an insulating effect on the body. To our knowledge, the largest intramuscular temperature reduction (1 cm depth) reported in the clinical literature is  $7^{\circ}\text{C}$ <sup>33</sup>; interestingly, this was observed with an 8-minute ice-pack application in a sample of healthy participants with very low levels of adipose tissue (0–10 mm skin folds at the site of application). We have also recently demonstrated<sup>34</sup> that the magnitude of temperature reduction also varies by body part, with bony regions such as the patella generally experiencing the largest reductions in tissue temperature.

## Adverse events

We found no evidence of adverse effects within the current review. However, in accordance with previous reviews in this area,<sup>4,35</sup> the majority of included studies did not seem to undertake active surveillance of predefined adverse events. Westerlund<sup>36</sup> noted that no adverse effects had occurred during 8 years of WBC use within a specialist hospital in Finland. In recent years, a small number of isolated problems associated with WBC (eg, skin burns on the foot) have been publicized within the media; these events have been attributed to oversights during preparation, such as entering the chamber with wet skin or clothing. The skin surface has been reported to freeze from  $-3.7^{\circ}\text{C}$  to  $-4.8^{\circ}\text{C}$ ,<sup>37</sup> with serious cellular damage and cryotherapy skin burns occurring at a threshold of around  $-10^{\circ}\text{C}$ .<sup>38</sup> As few studies have reported skin-temperature reductions beyond  $15^{\circ}\text{C}$  with WBC, excessive tissue-temperature reductions seem unlikely, provided adequate procedures for patient preparation are followed, and relevant contraindications are adhered to: uncontrolled hypertension, serious coronary disease, arrhythmia, circulatory disorders, Raynaud's phenomenon (white fingers), cold allergies, serious pulmonary disease, or the obstruction of the bronchus caused by the cold.<sup>36</sup>

## Biomarkers

There is evidence from animal models to suggest that cryotherapy can have a consistent effect on some important cellular and physiological events associated with inflammation after injury. These include cell metabolism, white blood cell activity within the vasculature, and potentially apoptosis.<sup>39–44</sup> Few studies have replicated these effects within human models. We highlighted two studies reporting an enhanced cytokine profile in athletes who used WBC after single<sup>7</sup> or multiple training exposures.<sup>8</sup> This should be regarded as preliminary evidence based on methodological limitations, including pseudorandomization and a risk of multiplicity. Others<sup>6,8,11</sup> found little effect of WBC on various markers of muscle damage after various forms of exercise training. Evidence from recent reviews suggests that CWI<sup>3</sup> and contrast water immersion<sup>35</sup> have little to no effect on markers of inflammation or muscle damage after exercise. To our knowledge, only one study has quantified the biochemical effects of local ice-pack application within human subjects with significant injury. Using the microdialysis technique, Stålman et al<sup>45</sup> reported that local icing and compression post-knee surgery resulted in a significantly lower production of prostaglandin  $\text{E}_2$  and synovial lactate compared to an untreated control group.



## Oxidative stress

There is evidence that CWI can induce oxidative stress and a possible increase in free radical species formation.<sup>46</sup> Free radicals are produced both as a by-product of cellular metabolism in aerobic systems and from various environmental sources. When free radical production exceeds antioxidant protection capacity and repair mechanisms, oxidative stress occurs, resulting in damage to such macromolecules as proteins, lipids, and deoxyribonucleic acid. The relative risk of oxidative stress appears to increase during periods of metabolic stress, where there is a disruption to the prooxidant/antioxidant equilibrium. A related concept is that brief repeated exposure to cold temperatures can benefit athletes by activating adaptive homeostatic mechanisms in accordance with the hormetic dose–response model.<sup>5</sup> Indeed, others have reported improvements in antioxidant capacity associated with regular exposure to cold-water swimming.<sup>46</sup>

Evidence from controlled studies on the effect of WBC on antioxidant capacity is equivocal. One study<sup>5</sup> reported a lower production of oxidative stress when intense exercise was undertaken in conjunction with WBC, compared to exercise alone. Surprisingly, these findings did not fully align with the athlete's antioxidant profiles, as the WBC group had a lower concentration of superoxide dismutase and glutathione peroxidase over the 10-day training period. Although Miller et al<sup>9</sup> found clearer evidence that WBC increases antioxidant activity in the absence of exercise, a limitation was that oxidative stress and antioxidant function were not quantified at the same site, and as such this makes it difficult to determine the mechanisms associated with oxidative stress. Furthermore, both these studies<sup>5,9</sup> quantified oxidative stress using the thiobarbituric acid reactive substances (TBARS) assay, which has a number of limitations.<sup>47</sup> For example, the TBARS assay claims to quantify the amount of malondialdehyde formed during the lipid-peroxidation process; a primary problem is that other substances such as biliverdin, glucose ribose, and 2-amino-pyrimidines all have the ability to be absorbed at or close to the same spectroscopic wavelength as TBARS (532 nm), and as such the assay generally reports inaccurate malondialdehyde concentrations when compared with more sophisticated techniques. Future studies should focus on the specific cell-signaling events leading to the increase in antioxidant protein expression and incorporate at least two or more indices of oxidative stress to confirm cell damage. In addition, direct measures of free radical production, such as electron paramagnetic resonance spectroscopy, would allow

for a more accurate quantification of free radical generation and oxidative damage.

## Autonomic nervous system

Finding efficient ways to influence the autonomic nervous system is a growing field in sports recovery. Intense exercise typically results in an increase in sympathetic activity, resulting in increased heart rate and decreased heart-rate variability. However, prolonged sympathetic activity is thought to be detrimental for postexercise recovery. As such, parasympathetic reactivation is currently considered to be an important indicator of systemic recovery, and often quantified using various indices of heart-rate variability.<sup>48</sup>

A small number of controlled studies have investigated the potential for using WBC to facilitate parasympathetic reactivation after exercise. Although there is evidence that WBC has an initial sympathetic effect,<sup>12</sup> its summative effect seems to be parasympathetic. Indeed, Schaal et al<sup>14</sup> reported that WBC enhances short-term autonomic recovery after intense exercise based on a two- to threefold increase in heart-rate variability. This response is thought to be mediated by the baroreflex, which is triggered by cold-induced vasoconstriction and an increase in central blood volume.<sup>49</sup> As such, parasympathetic reactivation is not exclusive to WBC, and others<sup>50–52</sup> have replicated these autonomic effects through CWI.

## Clinical outcomes

We found conflicting evidence for the effect of WBC on correlates of functional recovery following sport. There was however clearer evidence that WBC could improve subjective outcomes, such as perceived recovery and muscle soreness. This aligns with findings from a recent Cochrane review<sup>4</sup> concluding that CWI has little effect on recovery postinjury beyond reductions in muscle soreness. Similarly, although there is consistent evidence to show that cold packs and/or crushed ice provides effective short-term analgesia after acute soft-tissue injury and postsurgery,<sup>53–55</sup> there is little evidence to show any effect on functional restoration or swelling.

For the current review, we found one study<sup>13</sup> concluding that WBC has a clinically important effect on recovery from musculoskeletal injury (adhesive capsulitis). The underpinning mechanisms for these effects are difficult to determine. Perhaps an important consideration is that this study<sup>13</sup> used WBC in conjunction with standardized physiotherapy intervention involving manual therapy and joint mobilization.

It is possible that WBC produced a local analgesia, or acted as a counterirritant to pain, which facilitated mobilization. Optimal analgesia is associated with skin temperatures of less than 13°C,<sup>30</sup> a threshold that has been attained using standard WBC exposures in some reports.<sup>12,36</sup> We also know that WBC increases norepinephrine,<sup>2</sup> which could have an additional analgesic effect.<sup>56</sup> Local cooling can have an additional excitatory effect on muscle activation; this has been observed in both healthy and injured adults,<sup>57–60</sup> providing further evidence that cooling can be an important adjunct to therapeutic exercise.

## Benefits, harms, and recommendations for future research

When assessing therapeutic interventions, it is important to compare any benefits with possible risks and harms. In accordance with previous reviews,<sup>2</sup> we found that WBC can modify many important biochemical and physiological parameters in human athletes. We also found trends that WBC can improve subjective recovery and muscle soreness following metabolic or mechanical overload. This evidence should still be regarded as preliminary, and further high-quality randomized studies are recommended.

It is difficult to reach a definitive conclusion on possible risks associated with WBC, as studies have not undertaken active surveillance of predefined adverse events. This should be addressed within future studies; the constant pressure to maximize sporting performance means that athletes often experiment with extreme exposures and interventions. Current recommendations for WBC parameters, including optimal air temperatures and the duration and frequency of exposure, are largely based on anecdote. It is imperative that safe guidelines are developed using evidence-based information. Future studies should also determine whether it is necessary to alter the dose of therapy based on the nature of the injury, the severity, or the level of chronicity.

WBC is often regarded as a superior mode of cooling, due to its extreme temperatures. However, there is no strong evidence that it offers any distinct advantages over traditional methods of cryotherapy. There is much evidence to show that CWI and ice-pack application are both capable of inducing clinically relevant reductions in tissue temperature, and that they also provide important physiological and clinical effects.<sup>3,4,30,46,50,55</sup> Future research should directly compare the relative effectiveness of WBC, CWI, and ice-pack application. An important limitation is that WBC is currently significantly more expensive and much less accessible than either CWI or ice packs.

## Conclusion

WBC induces tissue-temperature reductions that are comparable to or less significant than traditional forms of cryotherapy. Controlled studies suggest that WBC could have a positive influence on inflammatory mediators, antioxidant capacity, and autonomic function during sporting recovery; however, these findings are preliminary. Although there is some evidence that WBC improves the perception of recovery and soreness after various sports and exercise, this does not seem to translate into enhanced functional recovery. Only one study has focused on recovery after significant musculoskeletal injury, and long-term implications are unclear. Until further research is available, athletes should remain cognizant that less expensive modes of cryotherapy, such as local ice-pack application or CWI, offer comparable physiological and clinical effects to WBC.

## Disclosure

The authors report no conflicts of interest in this work

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