

# Optimizing Cold Water Immersion for Exercise-Induced Hyperthermia: A Meta-analysis

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## ABSTRACT

ZHANG, Y., J.-K. DAVIS, D. J. CASA, and P. A. BISHOP. Optimizing Cold Water Immersion for Exercise-Induced Hyperthermia: A Meta-analysis. *Med. Sci. Sports Exerc.*, Vol. 47, No. 11, pp. 2464–2472, 2015. **Purpose:** Cold water immersion (CWI) provides rapid cooling in events of exertional heat stroke. Optimal procedures for CWI in the field are not well established. This meta-analysis aimed to provide structured analysis of the effectiveness of CWI on the cooling rate in healthy adults subjected to exercise-induced hyperthermia. **Methods:** An electronic search (December 2014) was conducted using the PubMed and Web of Science. The mean difference of the cooling rate between CWI and passive recovery was calculated. Pooled analyses were based on a random-effects model. Sources of heterogeneity were identified through a mixed-effects model  $Q$  statistic. Inferential statistics aggregated the CWI cooling rate for extrapolation. **Results:** Nineteen studies qualified for inclusion. Results demonstrate CWI elicited a significant effect: mean difference,  $0.03^{\circ}\text{C}\cdot\text{min}^{-1}$ ; 95% confidence interval,  $0.03\text{--}0.04^{\circ}\text{C}\cdot\text{min}^{-1}$ . A conservative, observed estimate of the CWI cooling rate was  $0.08^{\circ}\text{C}\cdot\text{min}^{-1}$  across various conditions. CWI cooled individuals twice as fast as passive recovery. Subgroup analyses revealed that cooling was more effective ( $Q$  test  $P < 0.10$ ) when preimmersion core temperature  $\geq 38.6^{\circ}\text{C}$ , immersion water temperature  $\leq 10^{\circ}\text{C}$ , ambient temperature  $\geq 20^{\circ}\text{C}$ , immersion duration  $\leq 10$  min, and using torso plus limbs immersion. There is insufficient evidence of effect using forearms/hands CWI for rapid cooling: mean difference,  $0.01^{\circ}\text{C}\cdot\text{min}^{-1}$ ; 95% confidence interval,  $-0.01^{\circ}\text{C}\cdot\text{min}^{-1}$  to  $0.04^{\circ}\text{C}\cdot\text{min}^{-1}$ . A combined data summary, pertaining to 607 subjects from 29 relevant studies, was presented for referencing the weighted cooling rate and recovery time, aiming for practitioners to better plan emergency procedures. **Conclusions:** An optimal procedure for yielding high cooling rates is proposed. Using prompt vigorous CWI should be encouraged for treating exercise-induced hyperthermia whenever possible, using cold water temperature (approximately  $10^{\circ}\text{C}$ ) and maximizing body surface contact (whole-body immersion). **Key Words:** COOLING, RECTAL TEMPERATURE, EXERTIONAL HEAT ILLNESS, SYSTEMATIC REVIEW

Heat illness resulting from prolonged hyperthermia is a common occurrence in sports and exercise (1). Exercise-induced hyperthermia has received sustained public attention over the past decade when large increases in cases of exertional heat stroke (EHS) deaths have been reported (4). A retrospective examination of 7-yr medical events involving 137,580 endurance runners indicates that fatal or life-threatening incidents were caused exclusively by EHS (63). Although the exact pathophysiology of fatal EHS remains unclear, our understanding is evolving (6,23). Recent evidence shows abnormally elevated

core temperature triggers inflammatory responses, causing irreversible and fatal EHS-associated multiorgan failure if treatment was delayed (24). After reviewing five fatal EHS cases in a single endurance race and one survival EHS case initially treated with ice water immersion, Rae et al. (50) commented that prompt initiation of active cooling is crucial for all suspected EHS. Immersion of body surface in cool, cold, or ice water, generally referred to as cold water immersion (CWI), has been suggested to be one of the most effective field cooling modalities (14,42). A cohort study summarizing 18 yr of hyperthermic runner records (18) supports the consensus view of implementing CWI as a criteria approach for the early treatment of EHS (14).

It is unquestionable that CWI is an effective method for rapidly cooling hyperthermic individuals, yet optimal evidence-based procedures for implementing CWI are not well established. First, although the existing guideline (14) has debated many criticisms of CWI and provided general guidance of care, limited numbers of studies at the time prevented previous reviews (14,42) from formulating specific recommendations regarding optimal procedures that could yield high cooling rates. A large number of significant

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evidences have been accumulated thereafter, and hence, a systematic review reflecting the latest evidences is needed for establishing the magnitude of the cooling rate and the precision around that magnitude. Second, current knowledge about the effectiveness of CWI was primarily based on small-sample size studies, and such results usually have low precision (i.e., wider confidence interval (CI)) on individual study basis and are not ideal for extending the applicability to the population at large. Suitable pooling of all relevant studies could increase power to improve precision. In life-saving situations, increased accuracy of the estimated cooling rate has practical significance to guide emergency procedures. Third, studies brought together in a systematic review inevitably differ in many ways (42). Many factors including water temperature used, body surface contact, severity of hyperthermia, and environmental conditions may play important roles in the effectiveness of CWI. Systematic analysis of the cooling rate allows the degree and reasons of discrepancy to be quantified and, if relevant, allows more reliable conclusions to be yielded. Fourth, previous evidence (50) supports the short period between the diagnosis of EHS and transportation of patients with EHS to hospital serves as a critical period for the early treatment of EHS (12). Practical difficulty in measuring core temperature in the field (34) calls the need for better prediction of recovery time, which is equally important in practice as pooled estimation of the cooling rate. Therefore, combining valid data from existing studies is valuable for standardizing the optimal procedures for the early treatment of exercise-induced hyperthermia, particularly EHS.

Accordingly, this meta-analysis synthesized the most relevant evidence on the effectiveness of CWI versus passive recovery conditions (i.e., lack of medical personnel, inaccurate temperature measurement, misdiagnosis, and/or inappropriate emergency treatments) (12,20,50,51) in terms of the cooling rate in healthy adults subjected to exercise-induced hyperthermia. This analysis should offer more precise guidelines for optimizing CWI use during emergency situations in sports as well as military and occupational settings.

## METHODS

**Literature search.** One investigator performed a computer-based search of the PubMed and Web of Science. The search phrases used were “cold water immersion,” “ice water immersion,” “ice bath,” “forearm immersion,” “immersion AND (Boolean connector) cooling,” which revealed 828 initial records. The titles and abstracts were reviewed on the basis of general inclusion criteria, as follows: English language, full-length articles published in peer-reviewed journals, healthy adults subjected to exercise-induced hyperthermia, and reporting core temperature as one outcome measure. Core temperature was limited to measurements either by rectal or telemetry pill thermometry rather than aural canal or esophageal thermometry, which present different temporal responses (28).

The application of these criteria refined the search results to 46 potential full-text articles, which were retrieved and thoroughly screened on the basis of specific exclusion criteria, as follows: core temperature at the commencement of CWI was below 38.3°C, having no passive recovery group, insufficient data for calculating the effect size, and/or duplicated results presented in another publication. When key information was not directly found in the original article, corresponding authors were contacted twice and were asked whether they would be willing to provide necessary information. Sixteen studies met the eligibility criteria. The literature search was enhanced by building citation maps from the references of each of the sixteen eligible studies, yielding 301 new records. After repeating the search procedure, another two eligible studies were revealed. One additional study was identified through another source. The search was completed in December 2014, identifying 19 eligible studies for the meta-analysis (3,10,15–17,19,25,29,33,35,44,46–48,53,58,61,62,65). A flow diagram illustrating the literature search process is presented in Figure 1.

To give a more informative view, those studies that meet all eligibility criteria except for not having a passive recovery group were also summarized (2,18,26,27,36–38,49,54,59). These studies were not entered in the meta-analysis.

**Data extraction.** One investigator extracted data. Data originally reported in the graphical form were digitally converted to numeric values (Photoshop version CC; Adobe).

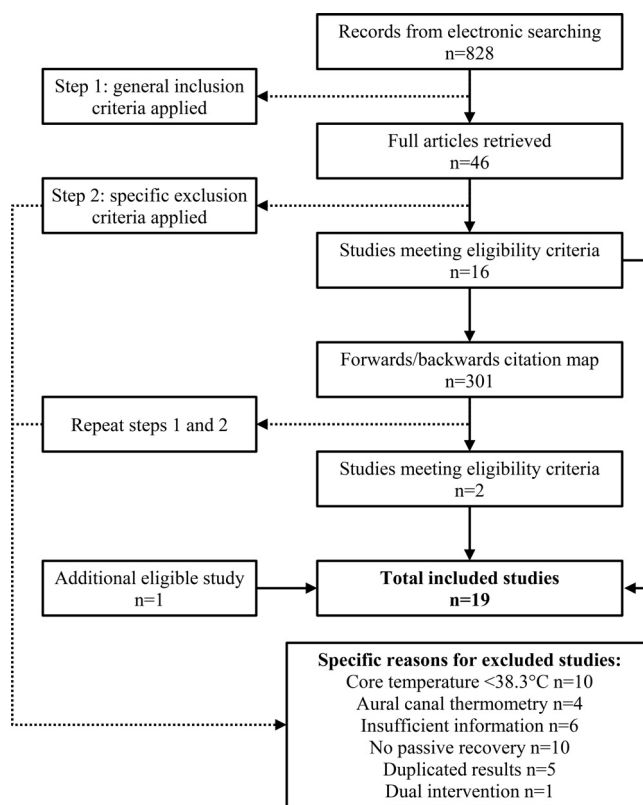


FIGURE 1—Flow diagram illustrating the study selection process.

The cooling rate was defined as reduction in the core temperature per unit of time during CWI or passive recovery.

Study characteristics were coded *a priori* as categorical variables for analyses. The coding was defined as follows: preimmersion core temperature (<38.6°C, ≥38.6°C), immersion water temperature (≤10°C, >10°C), ambient temperature (<20°C, 20°C–25°C, >25°C), immersion duration (≤10 min, 10–20 min, >20 min), and immersion level (forearms/hands, torso plus limbs).

Assessment of risk of bias within the studies was judged by two investigators working independently using the Physiotherapy Evidence-Based Database Scale (PEDro) (45). The range of the original score was 0–10, with a higher score indicating lower probability of bias. Because blinding was generally not practical in these studies, the scale with respect to blinding was not considered as a criteria of validity and the highest score that could be obtained was therefore 8. Any disagreements were resolved by a consensus between the two investigators.

**Meta-analysis.** Two levels of imputation were performed for missing data. First, among the included studies, four studies (44,46,47,53) did not report the SD of change from baseline core temperature. Using a borrowed intertrial correlation coefficient (*r*) of 0.85 (65), the SD of change from baseline

was imputed (31) and the cooling rate was calculated. Second, the within-subject *r* of crossover studies was calculated, yielding 0.18 (10) and 0.32 (19). A conservative *r* = 0.18 was assumed for reconstructing the SD of within-subject differences between CWI and passive recovery in crossover studies (22).

Meta-analyses were conducted using the Comprehensive Meta-Analysis (version 2.2; Biostat). Included in the meta-analysis were the mean differences in the cooling rate comparing CWI with passive recovery, along with 95% CI. CI not overlapping the null was considered a statistically significant effect. Data sets that investigated different immersion water temperatures were considered as independent mean differences (16); otherwise, data were transformed (30) to a single composite mean difference (25) to prevent bias toward anyone study's findings.

Because a common effect size cannot be assumed *a priori*, it was decided to use the random-effects model for the meta-analysis of all pooled data. Sensitivity analysis checked how imputations of missing data would have influenced the precision of the effect size. Heterogeneity was established computing the *I*<sup>2</sup> statistic (32). *I*<sup>2</sup> values of 25%, 50%, and 75% represent low, moderate, and high statistical heterogeneity, respectively. When inconsistency was observed, subgroup

TABLE 1. Characteristics of included (A) and excluded (B) studies

Citation	<i>n</i> <sup>a</sup>	Cooling Rate <sup>b</sup> (°C·min <sup>-1</sup> )		<i>T</i> <sub>w</sub> (°C)	<i>T</i> <sub>a</sub> (°C)	<i>t</i> (min)	<i>T</i> <sub>c</sub> (°C)	Immersion Level
		CWI	CON					
A. Included								
Barwood et al. (3)	9	0.04 ± 0.01	0.02 ± 0.02	17.8	31.2	15	38.7	Hands
Carter et al. (10)	10	0.04 ± 0.02	0.03 ± 0.02	12.5	15.0	20	38.5	Forearms and hands
Clapp et al. (15)	5	0.04 ± 0.02	0.01 ± 0.00	11.0	41.0	30	38.9	Torso
Clements et al. (16)	17	0.16 ± 0.04	0.10 ± 0.04	5.2	28.9	12	39.6	Shoulders to hip joints
		0.16 ± 0.04	0.10 ± 0.04	14.0				
Colburn et al. (17)	13	0.05 ± 0.04	0.03 ± 0.02	20.9	22.2	30	38.3	Forearm and hand
DeMartini et al. (19)	16	0.07 ± 0.03	0.04 ± 0.02	14.0	26.6	10	38.7	Whole body
Flouris et al. (25)	9	0.24 ± 0.10	0.03 ± 0.06	2.0	29.0	6.6	39.5	Whole body
Halson et al. (29)	11	0.09 ± 0.03	0.00 ± 0.00	11.5	24.2	3	38.9	Up to mesosternale
Hostler et al. (33)	17	0.05 ± 0.03	0.05 ± 0.03	14.3	24.0	20	38.3	Forearm and hand
Khomenok et al. (35)	17	0.05 ± 0.01	0.00 ± 0.00	10.0	35.0	10	38.3	Hands
Minett et al. (44)	9	0.04 ± 0.01	0.01 ± 0.01	10.0	32.0	20	38.4	Up to mesosternale
Peiffer et al. (46)	10	0.04 ± 0.01	0.03 ± 0.02	14.3	24.0	20	38.3	Up to midsternum
Peiffer et al. (47)	10	0.08 ± 0.05	0.00 ± 0.05	14.0	35.0	5	38.6	Up to midsternum
Pointon et al. (48)	10	0.09 ± 0.03	0.07 ± 0.02	8.9	32.4	18	39.1	Up to iliac crest
Robey et al. (53)	11	0.07 ± 0.00	0.04 ± 0.00	14.0	21.6	15	38.3	Up to midsternum
Taylor et al. (58)	8	0.18 ± 0.04	0.07 ± 0.01	14.0	21.0	2.2	40.1	Whole body
Walker et al. (61)	25	0.09 ± 0.07	0.06 ± 0.04	15.0	19.3	15	38.9	Up to umbilicus
Wyndham et al. (62)	6	0.04 ± 0.01	0.06 ± 0.01	14.4	21.1	60	40.0	Whole body
Zhang et al. (65)	7	0.05 ± 0.02	0.05 ± 0.01	12.0	20.7	15	39.0	Forearm and hand
B. Excluded								
Armstrong et al. (2)	14	0.20 ± 0.07	—	1–3	—	16	41.2	Torso and upper legs
Demartini et al. (18)	274	0.22 ± 0.11	—	10.0	—	—	41.4	Whole body
Friesen et al. (26)	20	0.22 ± 0.11	—	2.0	—	15.4	40.0	Up to nipples
Gagnon et al. (27)	10	0.14 ± 0.05	—	2.0	—	16.6	39.5	Whole body
Lee et al. (36)	4	0.19 ± 0.07	—	11.7	—	6	39.8	Up to sternums
Lemire et al. (37)	17	0.21 ± 0.09	—	8.0	—	12.9	40.0	Up to clavicles
Lemire et al. (38)	19	0.17 ± 0.07	—	2.0	—	14.7	39.5	Whole body
Proulx et al. (49)	7	0.35 ± 0.14	—	2.0	—	—	40.0	Up to clavicles
		0.19 ± 0.07	—	8.0	—	—		
		0.15 ± 0.06	—	14.0	—	—		
		0.19 ± 0.10	—	20.0	—	—		
Savage et al. (54)	12	0.05 ± 0.03	—	24.9	—	20	38.5	Forearms and hands
Vaile et al. (59)	10	0.09 ± 0.05	—	15.0	—	15	38.7	Whole body

<sup>a</sup>Total sample size in the CWI group.

<sup>b</sup>Data are expressed as mean ± SD.

CON, passive recovery; *t*, immersion duration; *T*<sub>w</sub>, immersion water temperature; *T*<sub>a</sub>, ambient temperature; and *T*<sub>c</sub>, preimmersion core temperature.

analysis based on a mixed-effects model  $Q$  statistic of homogeneity (5) was performed to identify sources of heterogeneity, with a cutoff significance level of 0.1 (32). The publication bias was visually inspected in the funnel plot and statistically tested using the Egger test (21).

**Inferential statistics.** On the basis of this meta-analysis, CWI data representing the 19 included and 10 excluded studies were pooled together to categorize the cooling rate for estimating recovery time. Akin to the meta-analysis, the computation contains two sources of variance. First, there is within-study random error in estimating the cooling rate in each study. Second, there is variation in the true cooling rate across studies. The random-effects model accounts for both uncertainties. Using a method of random-effects model, the inverse-variance weighted mean and 95% probability range were computed to indicate precision of the overall cooling rate.

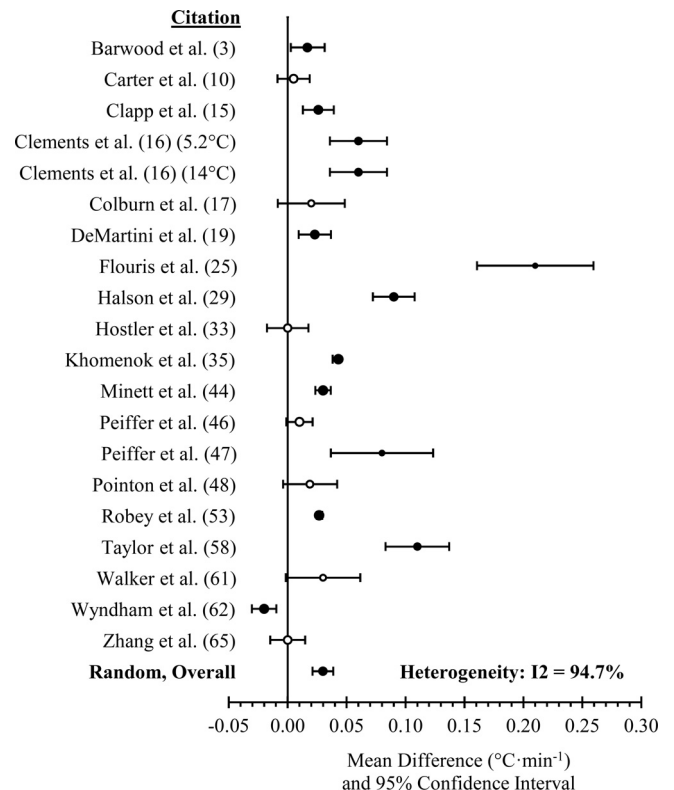
## RESULTS

Table 1A presents data from the 19 eligible studies in the meta-analysis. The mean  $\pm$  SD of the subject characteristics were as follows: age,  $26.4 \pm 4.9$  yr; height,  $178 \pm 4$  cm; body weight,  $75.7 \pm 5.3$  kg; and body surface area,  $1.9 \pm 0.1$  m<sup>2</sup>. The cooling rates were  $0.08^\circ\text{C}\cdot\text{min}^{-1} \pm 0.03^\circ\text{C}\cdot\text{min}^{-1}$  and  $0.04^\circ\text{C}\cdot\text{min}^{-1} \pm 0.02^\circ\text{C}\cdot\text{min}^{-1}$  for CWI and passive recovery, respectively. Except one study (62) that presents high risk of bias (PEDro score, 4), all included studies have PEDro scores ranging from 7 to 8. The descriptive data of the excluded studies are presented in Table 1B.

A forest plot displays mean differences and 95% CI for both individual studies and the meta-analysis (Fig. 2). CWI increased the cooling rate by  $0.03^\circ\text{C}\cdot\text{min}^{-1}$  (95% CI,  $0.03$ – $0.04^\circ\text{C}\cdot\text{min}^{-1}$ ) compared with passive recovery. By removing the four studies with imputed SD from the analysis, the mean difference was  $0.04^\circ\text{C}\cdot\text{min}^{-1}$  (95% CI,  $0.02$ – $0.05^\circ\text{C}\cdot\text{min}^{-1}$ ). By assuming  $r = 0$  in crossover studies, the result did not shift. As such, sensitivity analysis confirms there is minimal effect of imputations on the result.

High statistical heterogeneity presents across studies, justifying the subgroup analysis. There are significant increases ( $P < 0.10$ ) in the cooling rate when preimmersion core temperature  $\geq 38.6^\circ\text{C}$ , immersion water temperature  $\leq 10^\circ\text{C}$ , ambient temperature  $\geq 20^\circ\text{C}$ , and immersion duration  $\leq 10$  min (Fig. 3). Furthermore, the cooling rate of torso plus limbs immersion (mean difference,  $0.04^\circ\text{C}\cdot\text{min}^{-1}$ ; 95% CI,  $0.03$ – $0.06^\circ\text{C}\cdot\text{min}^{-1}$ ) was higher ( $P = 0.028$ ) than that of forearms/hands immersion (mean difference,  $0.01^\circ\text{C}\cdot\text{min}^{-1}$ ; 95% CI,  $-0.01^\circ\text{C}\cdot\text{min}^{-1}$  to  $0.04^\circ\text{C}\cdot\text{min}^{-1}$ ).

Visual inspection of the funnel plot indicates no obvious asymmetry (Fig. 4). This interpretation is confirmed by the Egger test, with a regression intercept  $P = 0.40$  (one tailed), suggesting low probability of publication bias. Built on the preceding subgroup analysis, the weighted cooling rate of CWI based on 29 relevant studies is categorized in Table 2,



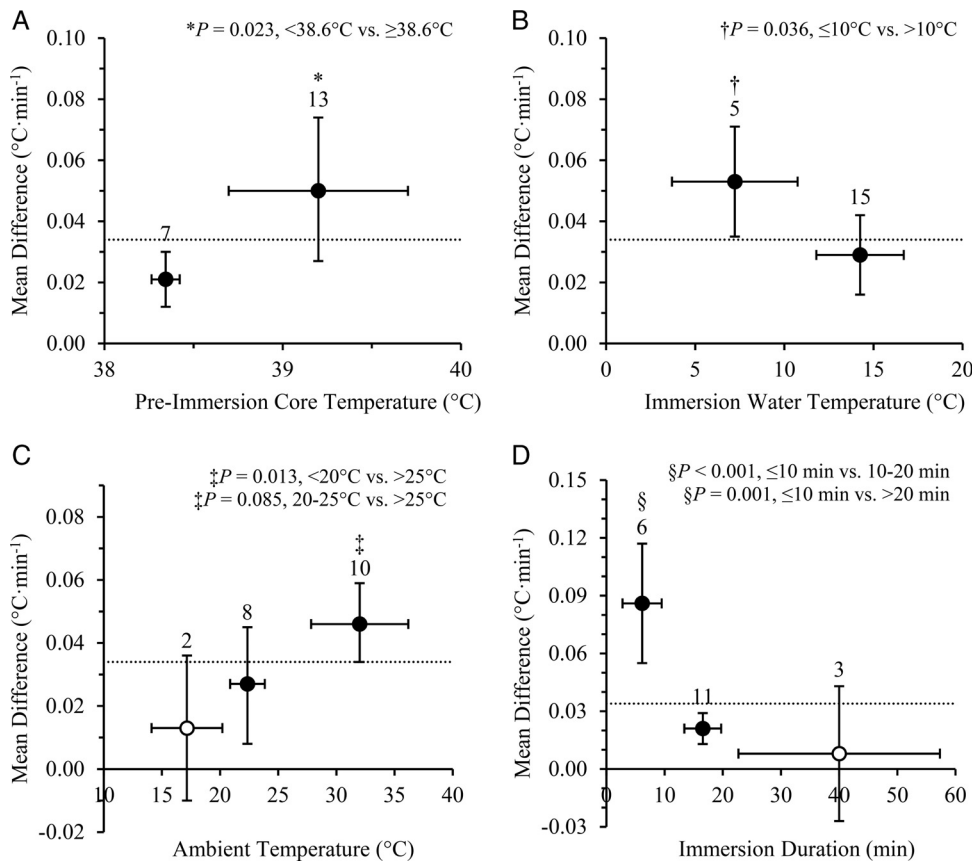
**FIGURE 2**—Forest plot displaying the effect of CWI vs passive recovery on the cooling rate. The horizontal line depicts the 95% CI. The circle size indicates the weight assigned to the included studies in the meta-analysis. Open circles represent insignificant effect, whereas filled circles represent significant effect.

along with the estimated recovery time for commonly used CWI settings in the field.

## DISCUSSION

This meta-analysis has quantified several key factors that contribute to the effectiveness of CWI, aiming to provide evidence-based suggestions for optimizing field practice of CWI. Empirical data support that CWI results in faster cooling rates compared with passive recovery, and greater cooling rates with CWI would be expected to lead to better outcomes in treatment of EHS. Quantitative analysis strengthens the existing knowledge by identifying the key elements that could make justifiable broad generalizations. Moreover, it seems that using forearm/hand CWI as a rapid cooling modality for treating severe exertional hyperthermia warrants reconsideration. Finally, aggregated CWI data are of vitally practical significance to guide emergency procedures.

Overall, data show that CWI yields a twofold-greater rate of cooling than passive recovery. This  $0.08^\circ\text{C}\cdot\text{min}^{-1}$  cooling rate, however, is less than the current guideline for treating EHS (14), of which a minimum cooling rate of  $0.1^\circ\text{C}\cdot\text{min}^{-1}$  is required immediately upon diagnosis of EHS. The ultimate goal of cooling is to rapidly restore homeostasis in critical organs, regardless of treatments or



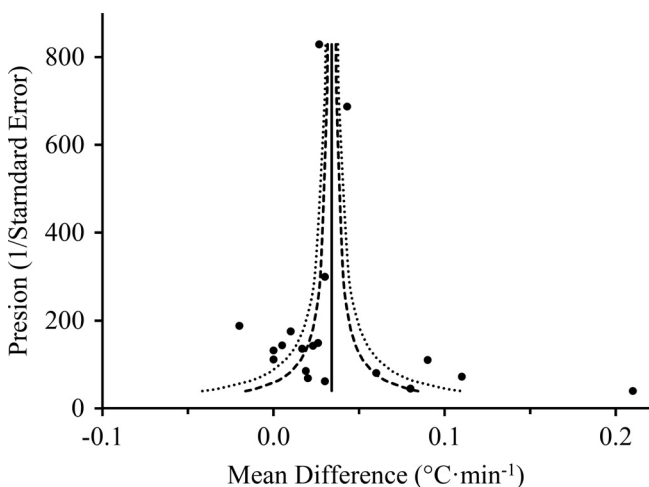
**FIGURE 3**—Subgroup analyses displaying the effect of CWI vs passive recovery on the cooling rate. On the abscissae, the mean differences in the cooling rate with 95% CI are presented and on the ordinate showing mean and SD of covariables, with number of studies in each analysis shown on the top. Dashed lines show the mean difference ( $0.034^{\circ}\text{C}\cdot\text{min}^{-1}$ ) of the included studies in the meta-analysis. Open circles represent insignificant effect, whereas filled circles represent significant effect. The  $Q$  statistic  $P$  value is indicated when significant subgroup homogeneity is observed.

environmental conditions in which it is undertaken. This moderate improvement is not without practical importance; rather, CWI is a very effective cooling modality, especially taking into account that it cools twice as fast as passive

recovery. In events of possible fatal EHS, such an advantage should not be underappreciated.

Although no evidence of publication bias was shown in the meta-analysis, this should not be taken as evidence of no bias. Because of the methodological limitation, this meta-analysis *a priori* excluded a number of CWI studies without a passive recovery group, among which some very high cooling rates were reported. For example, Lemire et al. (37) investigated  $8^{\circ}\text{C}$  CWI and the cooling rate was  $0.21^{\circ}\text{C}\cdot\text{min}^{-1}$  (95% CI,  $0.16\text{--}0.26^{\circ}\text{C}\cdot\text{min}^{-1}$ ). Friesen et al. (26) showed a cooling rate of  $0.22^{\circ}\text{C}\cdot\text{min}^{-1}$  (95% CI,  $0.17\text{--}0.27^{\circ}\text{C}\cdot\text{min}^{-1}$ ) using  $2^{\circ}\text{C}$  CWI. The advantage of CWI has been shown clearly by Armstrong et al. (2), in which hyperthermic runners were successfully cooled using  $1^{\circ}\text{C}\text{--}3^{\circ}\text{C}$  CWI and the observed cooling rate was  $0.2^{\circ}\text{C}\cdot\text{min}^{-1}$  (95% CI,  $0.17\text{--}0.23^{\circ}\text{C}\cdot\text{min}^{-1}$ ). This methodology-associated drawback that precludes all relevant studies for the meta-analysis should be noted. Thus, the cooling rate in this meta-analysis may underestimate the true effect size and potentially devalue the superiority of CWI; nonetheless, it is clearly an effective cooling modality.

Cooling seems to be more effective when preimmersion core temperature was  $\geq 38.6^{\circ}\text{C}$  and during the initial 10-min immersion. The observation does not depart from the literature



**FIGURE 4**—Funnel plot displaying the mean differences in the cooling rate and the inverse of SE for the included studies in the meta-analysis. The vertical line marks the weighted mean difference, and the dashed lines represent 2- and 3-sigma intervals.

TABLE 2. Weighted CWI cooling rate synthesized from 29 studies and projected time to cool core temperature by 1°C.

(°C·min <sup>-1</sup> )	Cooling Rate (min)	1°C Time
Core temperature		
≤39°C	0.06 (0.05–0.06)	18 (16–21)
39°C–40°C	0.17 (0.13–0.22)	6 (5–8)
>40°C	0.20 (0.18–0.23)	5 (4–6)
Water temperature		
≤5°C	0.21 (0.17–0.25)	5 (4–6)
5°C–10°C	0.13 (0.09–0.18)	8 (6–11)
>10°C	0.08 (0.07–0.09)	13 (11–15)
Immersion duration		
≤10 min	0.12 (0.08–0.15)	9 (7–12)
10–20 min	0.10 (0.08–0.11)	10 (9–12)
>20 min	0.04 (0.03–0.05)	24 (21–29)
Immersion level		
Torso plus limbs	0.13 (0.11–0.15)	8 (7–9)
Forearms/hands	0.05 (0.04–0.05)	22 (20–24)

The 29 studies are summarized in Table 1. Values in parentheses are the 95% probability range.

(16,54). First, on the basis of the Newton law of cooling, higher onset core temperature elicits greater capacity of heat sink, thus potentially augmenting the cooling rate. Secondly, cardiovascular manifestations during heat strain show that hot skin increases the demand of the skin blood flow in maintaining homeostasis (55). The study by Mawhinney et al. (40) gives insight into this area, in which significant reductions in the skin temperature and skin blood flow were observed after 10-min 8°C CWI from an onset core temperature of approximately 37.8°C, indicating a probable reduction in heat transfer capacity. This may partially explain the result that CWI was more effective during the initial 10-min immersion. Collectively, it would be expected that a combination of high core (>40°C) and skin (>37°C) temperatures in individuals developing symptoms of exertional heat illness could likely augment the motor drive for cooling. A large cohort study illustrated this phenomenon, showing the highest recorded cooling rate of 0.6°C·min<sup>-1</sup>, when a heat-injured runner with an onset core temperature of 42.2°C was immersed into approximately 10°C cold water (18). Indeed, this supports the mentioned conjecture that the effectiveness of CWI interrelates with the severity of hyperthermia. In this regard, this assumption also holds that the cooling rate of CWI progressively decays for which an effective cooling should be yielded no longer than 20 min of immersion, especially, during the initial 10 min.

The result demonstrates that the most effective water temperature for CWI would be ≤10°C cold water, and likely, the colder, the better. Immersion in 2°C ice water usually provided desirable high cooling rate (26,38), as high as 0.35°C·min<sup>-1</sup> (95% CI, 0.22–0.48°C·min<sup>-1</sup>) using circulated water bath (49). On this basis, the use of ice water seems genuinely advantageous for rapid restoration of homeostasis. Our experience with CWI suggests that achieving water temperatures <5°C in tanks large enough for whole-body immersion requires large quantities of ice and stirring. Achieving these temperatures in the field and having such cooling immediately available could be challenging. Therefore, immersion in <5°C ice water may not be a viable

practical option particularly in field settings. However, 5°C–10°C ice water might be achieved in the field, and a severe EHS case (50) supports the argument that this water temperature range is tolerable and, more importantly, crucially contributes to survival (13). Nevertheless, more convenient yet effective protocol could be achieved with the use of approximately 10°C CWI. The most compelling evidence is the finding that using approximately 10°C CWI resulted in a 100% survival rate for EHS runners (18). The use of approximately 10°C CWI is logistically manageable and empirically supported and thus should be undoubtedly embraced.

Insights into the practical application of the current findings can further be gleaned from consideration of ambient temperature. The cooling rates of passive recovery via convection, radiation, and evaporation were significantly lowered at ≥20°C ambient temperature, reflecting that the effectiveness of passive recovery is highly dependent upon environmental conditions. Exertional hyperthermia and EHS occur not only in warm/hot and humid environments but also in cool and dry environments (52,60). Even though the result shows that passive recovery is effective when ambient temperature drops below 20°C, using CWI should not be discouraged. No data are available to prove that passive recovery could assure zero mortality; in contrast, active cold water cooling achieved a 100% survival rate in cool environments (43). On the other hand, it can be clearly interpreted that CWI should be prepared in advance when sports events, endurance type in particular, occur at ≥20°C ambient temperature. In events of EHS, delayed treatment may lead to fatal outcomes, and hence, effective field cooling modalities such as CWI must be readily available and immediately initiated in the “golden half-hour” (12).

The immersion level further distinguishes the cooling rate of torso plus limbs immersion from that of forearms/hands immersion. This issue concerns with conductive heat transfer; thus, not surprisingly, more body surface contact is naturally more efficient for heat dissipation (64). It can be assumed that the cooling rate speeds up along with the increase in body surface contact during CWI. Torso immersion, ideally whole-body immersion, shows great promise for rapid cooling and hence should be recommended regardless of immersion water temperature.

Remarkably, there is insufficient evidence to show that forearm/hand CWI provides rapid cooling. The origin of forearm/hand cooling can be traced to the early study of Livingstone et al. (39). Livingstone et al. (39) compared different immersion water temperatures, and their cooling rates were similar across different cooling temperatures and passive recovery. Because of the difference in temporal responses (28), studies exploring forearm/hand CWI on the basis of the aural canal or esophageal thermometry were not incorporated in this meta-analysis. In view of rapid cooling based on the rectal thermometry, however, there is limited evidence showing substantial effect of forearm/hand CWI (3,35) over passive recovery and the usefulness of this

method is in doubt. The current observation should not be viewed as a refutation of forearm/hand CWI as an effective rehabilitation modality because there are other associated benefits (8,56,65). Yet, insufficient published evidence supports that forearm/hand CWI could yield desirable rapid cooling. Regardless of whether natural evaporative or convective cooling is adequate or impeded (via wearing of protective clothing and/or high ambient temperature and humidity), individuals can still be overwhelmed in cases of severe exertional hyperthermia.

Because of ethical reasons, the included studies have only addressed moderate hyperthermia in healthy individuals, and all guidelines proposed here may not apply to EHS or classical hyperthermia. The subjects in laboratory studies likely maintained intact homeostatic systems despite moderately elevated core temperature and hence may have experienced transient vasoconstriction during the course of CWI (14). Conversely, hyperthermic patients with heat injury might not exhibit normal vasoconstriction (14) and thereby achieve more rapid cooling. If true, then the cooling rate from this meta-analysis should be viewed as conservative, observed estimates and likely might be boosted when the body's homeostasis is more challenged (core temperature,  $>40^{\circ}\text{C}$ ).

Whereas extremely elevated core temperature in normotensive and non-EHS individuals could gradually return to normothermia after a period of passive recovery, conventional thermoregulatory mechanisms fail in patients with EHS. There is accumulating evidence showing that commonly encountered complications in EHS include circulatory collapse and postexercise endogenous heat production (7,23,24,50), highlighting that conventional thermoregulation via convection and evaporation is greatly challenged. Eventually, this leads to thermoregulatory failure and further promotes persistent hyperthermia (23). In this meta-analysis, CWI was compared against passive recovery to establish the magnitude of the cooling rate. From the available evidence, it can be assumed that the computation is statistically correct yet ecologically invalid because of thermoregulatory failure in EHS situations. In circumstances of overwhelmed thermoregulatory mechanisms, heat loss in patients with EHS heavily, if not solely, relies on conduction. Establishing the greatest core-to-water temperature gradient and maximizing body surface contact as possible during CWI is clearly necessary for rapidly cooling patients with severe EHS.

While practitioners await an enduring principle shift in the field (34), fatal EHS can clearly be treated and minimized with proper CWI (18,50). Aggregated data presented in Table 2, pertaining to 607 subjects from 29 studies, can be readily adopted by practitioners as a useful framework for implementing CWI. Two notions are worth mentioning for better application of the proposed data in the field. First, the successful use of rectal temperature in diagnosing EHS cases (18) proves its value in the field and hence should be impartially recommended. Recent findings have found that some healthcare providers considered the use of rectal temperature impractical in field settings (41), but these concerns

could jeopardize appropriate care for patients with EHS. Alternatively, measurement of core temperature in mass participation sporting events could be achieved via telemetry pill thermometry (9,11) albeit at a cost and subject to thermal variation (57). Nonetheless, if measuring core temperature is not feasible in the field, it is suggested to cool no more than  $3^{\circ}\text{C}$  to prevent overcooling (27), assuming that severe exertional heat illness and EHS typically occur at a rectal temperature of approximately  $41.5^{\circ}\text{C}$  (95% CI,  $41.2^{\circ}\text{C}$ – $41.9^{\circ}\text{C}$ ) (50). The proposed recovery time offers practical references of time to restore nonthreatening core temperature in suspected EHS. Second, although the proposed data are summarized from a large body of records, the validity is subject to the severity of hyperthermia. Patients with EHS may show extreme resistance to cooling (7,24), and the effectiveness of CWI has been reported to be only 20% of the expected cooling rate (50). Thus, practitioners should bear in mind that the effectiveness of CWI may be hampered by acute circulatory collapse and/or excessive endogenous heat production in patients with EHS and the proposed cooling rate and recovery time should be interpreted with great caution. A rule of thumb is to continuously monitor body temperature, preferably rectal temperature if feasible, during the entire period of emergency treatment and rehabilitation care.

## CONCLUSIONS

This meta-analysis has quantified the prescription of key elements of CWI and provided the current best evidence-based suggestions. This generalization is further enhanced by considering evidences from both laboratory non-EHS and clinical EHS records. In conclusion, a clear guideline regarding the optimal cooling procedure is proposed as follows: 1) be ready to implement CWI when endurance events take place at  $\geq 20^{\circ}\text{C}$  ambient temperature, 2) continuous exposure in approximately  $10^{\circ}\text{C}$  cold water is a proven method, but be ready to implement even larger core-to-water temperature gradient for treating patients with severe EHS, 3) whole-body CWI can maximize the conductive heat dissipation while forearm/hand CWI is insufficient for rapid cooling, and 4) when measuring core temperature is (commonly) not feasible in the field during suspected EHS, assume  $41.5^{\circ}\text{C}$  as the start point of core temperature and  $38.6^{\circ}\text{C}$  as an acceptable cessation point (27) to implement CWI, ideally within 20 min of immersion, and apply the proposed recovery time to guide active cooling before advanced emergency supports arrive.

The recovery intervention of CWI has been repeatedly proven to be a criteria approach in the realm of exercise-induced hyperthermia. Rather, the future lies in adopting the previous (14) and currently proposed guidelines and planning emergency procedures in the field. All efforts should be made to continuously educate physicians, athletic trainers, sports organizers, and relevant practitioners concerning the optimal procedures of CWI when exercising or working in challenging environments.

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