Heat acclimation for protection from exertional heat stress (Protocol)

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[Intervention Protocol]

Heat acclimation for protection from exertional heat stress

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

To assess the effects of heat acclimation interventions aimed at protecting health and performance from exertional heat stress.

BACKGROUND

Description of the condition

High ambient temperatures and relative humidities increase metabolic heat gain accompanying exercise and are associated with increased physiological strain and reduced physical work capacity (Wendt 2007). Indeed, wherever excessive imbalances occur between the thermal energy stored and that dissipated to the environment, heat-related illness can occur. Often referred to as heat injury, heat-related illnesses describe a range of conditions that include heat rash (miliaria rubra), fluid retention, muscle cramp, fainting, heat exhaustion and heat stroke (Bouchama 2002). In extreme cases, excessive rises in core temperature above 40° C result in central nervous system dysfunction, cellular death and multiple organ failure (Coris 2004; Glazer 2005; Sharma 2003). The young and elderly may be vulnerable to extreme heat events (Kovats 2008), though heat illnesses associated with physical exertion are also experienced by athletes, manual labourers and military personnel, particularly when not acclimatised (Bouchama 2002).

The health and financial effects of heat-related illness on everyday life as well as occupational and sports settings are rising, as the increased intensity, duration and frequency of heat wave conditions associated with global climate change take effect (Huang 2011; Luber 2008). Chinese data highlight a 4.5% increase in hospital admission rates with every 1° C increase in mean daily temperature above 29° C (Chan 2013), with similar trends reported in Australia (Bi 2011) and the United States of America (USA) (Green 2010). Compounding this elevated burden on the healthcare sector, modelling by Dunne 2013 indicates heat stress to have impaired global labour capacity by up to 10% in recent decades, with this likely to double in peak summer by 2020. The economic consequences of this reduced work are marked, with

estimated net costs of USD 2.4 trillion by 2030 attributed to heat-related reductions in work productivity alone (DARA 2012).

Although the risk of exertional heat illness may be reduced by using air conditioning, scheduling physical activity in the coolest time of the day and maintaining adequate hydration (Gupta 2012; Michelozzi 2014), accustomed exposure to hot weather is not always possible. For example, variability in extreme weather patterns (i.e. El Niño and La Niña) (McGeehin 2001), inter-seasonal travel (Hanna 2011), geographic location (Grundstein 2015), and the need for protective equipment in occupational, military, and sporting contexts (Cheung 2000; Holmér 2006; Montain 1994) each unavoidably increase thermal strain.

Heat acclimation is regarded as the most effective means of protecting health against thermal strain. It involves a series of (natural or artificial) exposures to hot conditions in order to invoke physiological adaptations that optimise heat loss mechanisms (Taylor 2006). Importantly, enhanced thermoregulatory efficiency achieved through acclimation may maintain work rate in hot conditions (Chalmers 2014; Lorenzo 2010) and is included in health and safety recommendations for various sports, occupational and military populations (CA DoOSH 2015; Racinais 2015; US Army 2003).

Description of the intervention

Heat acclimation involves a series of adaptations that reduce physiological strain in hot conditions by optimising avenues for heat loss. The treatment requires repeated exposures to an elevated body temperature that can be achieved using passive (i.e. non-active heat absorption from the surrounding environment), active (i.e. heat production caused by greater energy metabolism during exercise), or combinations of both methods. Passive heat acclimation methods include using climate chambers, saunas, water baths and vapour barrier suits (e.g. Fox 1963; Scoon 2007; Stanley 2015; Zurawlew 2015). Exercise-induced heat acclimation may be achieved using constant work-rate (fixed duration or controlled hyperthermia) or self-paced exercise protocols that are usually undertaken in environmental conditions that are hot or humid or both (e.g. Armstrong 1986; Garrett 2009; Gibson 2015; Houmard 1990).Typically, these exposures are administered for 30 to 120 minutes and are repeated across multiple days. Accepted definitions of heat acclimation processes are: up to seven exposures (short-term heat acclimation), eight to 14 exposures (medium-term heat acclimation), and 15 or more exposures (long-term heat acclimation) (Chalmers 2014; Garrett 2011). Adaptations to heat exposure is never permanent. According to Givoni 1973, heat adaptation is lost every day spent without heat exposure at a rate that is twice as fast as the rate with which the heat adaptation was initially gained.

Recommendations for athletes to follow heat acclimation protocols have become increasingly common as a means to protect both health and physical performance during major competitions in hot environments (Chalmers 2014; Guy 2015; Racinais 2015). Occupational safety and health concerns regarding heat-related illness in industry (e.g. military, agriculture, construction, landscaping, oil and gas extraction, and transport) have also led to state-legislated standards that emphasise acclimation (or acclimatization) awareness in the USA (CA DoOSH 2015; Washington State Legislature 2012). However, even in the South African mining industry, where evidence for the use of heat acclimation interventions is long standing (Wyndham 1969), consensus on evidence-based best practice remains elusive. Regardless, to optimise the heat acclimation response, all variables (e.g. environmental temperature and humidity, exercise mode, exercise intensity, exposure duration and number of exposures) should be considered within the logistical and economic constraints of the setting.

How the intervention might work

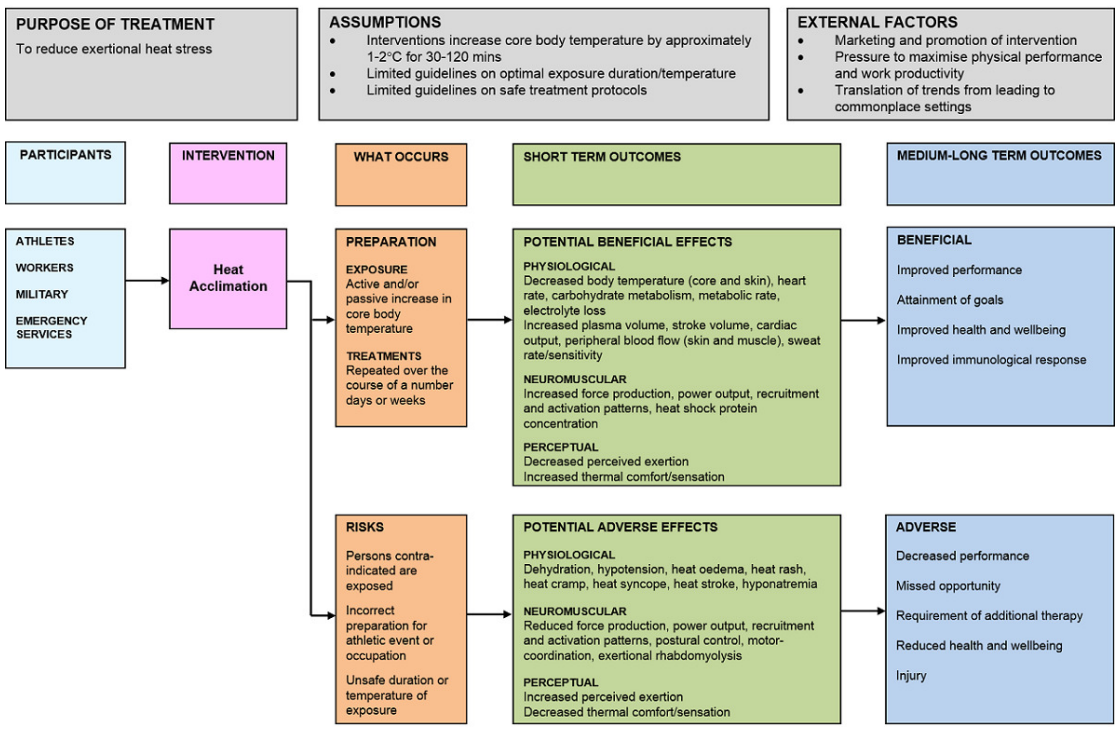
Humans regulate core temperature through changes in autonomic (e.g. sweating and shivering) and behavioural (e.g. work rate) thermo-effector responses (Cabanac 1977; Hartley 2012; Schlader 2009). During physical exertion in hot conditions, heat is gained through both endogenous (i.e. increased metabolism required to complete work) and exogenous sources (i.e. transferred from the surrounding environment) (Wendt 2007). The maintenance of core temperature within a homeostatic range at rest (~36.8 ± 0.5 ° C) (Hanna 2015) is mostly achieved via convection of heat to the skin surface and radiation of heat to the surrounding environment (Sawka 1996). However, once core temperature meets or exceeds that of the external environment, sweating provides the main heat loss mechanism through evaporation (Sawka 1996). Relative humidity, air flow and skin exposure to the external environment all influence evaporative heat loss and when compromised (e.g. when wearing personal protective equipment), exacerbates heat strain and leads to people working slower or for shorted periods of time to avoid excessive thermal injury (Marino 2004; Tatterson 2000; Tucker 2006).

Notably, repeated exposures to an increased core temperature achieved via exercise, environmental means, or both, induce physiological adaptations associated with greater thermal tolerance (Armstrong 1991; Garrett 2011; Taylor 2006). Acclimation to a hot environment evokes a complex multi-system response that results in improved rates of heat loss that are associated with cardiovascular, endocrine and nervous system changes (Francesconi 1996). The classic signs of heat acclimation include a lowered heart rate, cooler body temperature (core and skin), and earlier and larger sweat responses to exercise in hot conditions (Sawka 1996). These adaptations may be associated with plasma volume expansion stimulated by repeated heat exposures (Nielsen 1993; Patterson 2004; Senay 1976), which are attained via altered kidney function that maintains body water and electrolyte concentrations (Francesconi 1996). This allows for the maintenance of

skeletal muscle blood flow during exercise (Chalmers 2014) and evaporative cooling by sweating (Libert 1983; Nadel 1974), while reducing the risk of dehydration.

The physiological adaptations experienced during heat acclimation markedly enhance thermal comfort (Daanen 2011; Petersen 2010; Sunderland 2008) and lower ratings of perceived exertion in hot conditions (Armstrong 1991; Castle 2011; Pandolf 1977). This is key as the combination of both lowered physiological and perceptual demands allow for longer tolerance times and more work to be completed in the heat (Chalmers 2014; Lorenzo 2010). However, physiological adaptations are variable depending on acclimation mode, duration and frequency, and individual responses will impact subsequent thermal tolerance and physical performance (Lambert 2008; Racinais 2012; Racinais 2014). Moreover, it should be noted that the protective and performance benefits of heat acclimation are limited (Hanna 2015), and in extreme weather, high task motivation or confidence in heat tolerance or both should not come at the expense of appropriate work-rest schedules (Lucas 2014). To guide the scope of the review, we developed a logic model (Figure 1) in accordance with Anderson 2011 that outlines: 1) potential benefits and 2) adverse effects of heat acclimation interventions in alleviating exertional heat stress.

Figure 1. Logic model describing the potential benefits and adverse effects of heat acclimation



Why it is important to do this review

Exertional heat illness is a major concern amongst applied practitioners (Casa 2015) and its rising incidence rate in physically active populations is likely to be exacerbated as global warming continues (Brocherie 2015; Lucas 2014; Mueller 2012). Considering the health concerns and the associated costs to industry and government, it is important that there are evidence-based guidelines to best inform heat acclimation procedures (Taylor 2006). The effects of heat stress on active paediatric and adolescent populations have been given a lot of attention (Bergeron 2011; Casa 2009; Marshall 2010). However, there are no practical recommendations available that are based on empirical evidence (Armstrong 2007; Bergeron 2005). A recent systematic review and meta-analysis of eight small studies (including six observational and two randomised controlled trials) reported short-term heat acclimation ($\leq$ 7 exposures) to increase aerobic performance outcomes (Chalmers 2014). While Chalmers 2014 has practical implications for athletes and coaches involved in team sports, outcome mea-

sures were restricted to athletic performance only. Applications of the heat stress Standard ISO 7243 indicate greater work tolerance of a high wet bulb globe temperature (i.e. a heat stress index that incorporates temperature, humidity and radiation) following acclimation (Parsons 2006), without detailing how this is achieved. Accordingly, questions remain as to the optimal dosage effects of heat acclimation, underlying mechanisms, and the potential for adverse outcomes on health and performance across all populations and contexts (e.g. occupational, military, and sports).

OBJECTIVES

To assess the effects of heat acclimation interventions aimed at protecting health and performance from exertional heat stress.

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomised controlled trials (RCTs) and quasi-RCTs. Quasi-RCTs will be included to incorporate field-based studies whereby true randomisation is practically difficult (e.g. when the intervention is administered to a group of workers). We will include studies reported as full-text, those published as abstract only, and unpublished data.

Types of participants

We will include studies conducted with adult participants (aged 18 or above), with no restrictions on gender, type or level of exercise or physical activity. We will include relevant field- and laboratory-based trials in which the participants are apparently healthy. We anticipate that people who have a recent history of injury or any contraindication to heat acclimation will be excluded from the original trials.

Types of interventions

We will include trials that have evaluated the effectiveness of heat acclimation, defined as the process of deliberately administering repeated heat exposures to improve thermal tolerance in hot conditions. We will include all forms of heat acclimation (i.e. active and passive) in the review. No restrictions will be placed on frequency, dose, or duration of the intervention.

We will include studies comparing heat acclimation interventions and a control (no intervention), as well as those comparing different acute heat acclimation interventions (varying in frequency, dose and duration). We will also include studies comparing heat acclimation interventions and any other intervention aimed to prevent exercise- and environment-induced heat stress, including:

- Aerobic fitness training;
- Hydration strategies (hyper- or hypohydration);
- Pre-cooling (body cooling before exercise);
- Nutritional and pharmacological supplements;
- Body composition alterations; and
- Sleep hygiene.

We will exclude trials in which the same heat acclimation protocol is used in both arms as a co-intervention. We will also exclude interventions involving multiple strategies to optimise health and performance in hot conditions where the effects of heat acclimation cannot be differentiated from the effects of the other strategies.

Types of outcome measures

Primary outcomes

1. Core temperature (e.g. rectal, aural and oesophageal)
2. Physical performance (e.g. VO_{2max}, time trial, tolerance time, muscle strength or power)
3. Complications or adverse health effects as reported by the individual trials (e.g. heat-related illness or injury)

We will exclude trials that do not report any of the primary outcomes.

Secondary outcomes

1. Heart rate
2. Skin temperature
3. Plasma volume
4. Sweat rate
5. Perceived exertion
6. Thermal sensation or comfort

Timing of outcome measures

We plan to examine the effectiveness of outcome measures on the basis of changes detected in post-intervention measures with a control or another intervention. Where experimental designs allow, we also plan to extract data post-intervention to examine the time course of acclimation decay. We expect that few studies will report multiple post-intervention measures. However, of those that do, a four week follow-up time is the typical maximal duration of studies examining acclimation decay (Armstrong 1991; Weller 2007).

Search methods for identification of studies

We will not restrict our search by language, date or publication status.

Electronic searches

The Cochrane Injuries Group Trials Search Co-ordinator will search the following:

1. Cochrane Injuries Group specialised register (present version);
2. Cochrane Central Register of Controlled Trials (CENTRAL, *The Cochrane Library*) (latest issue);
3. Ovid MEDLINE(R), Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid OLDMEDLINE(R) (1946 to present);
4. EMBASE Classic + EMBASE (OvidSP) (1947 to present);
5. PubMed (limited to non-MEDLINE indexed publications);
6. ISI Web of Science: Science Citation Index Expanded (SCI-EXPANDED) (1970 to present);
7. ISI Web of Science: Conference Proceedings Citation Index-Science (CPCI-S) (1990 to present);
8. CINAHL Plus (EBSCO) (1937 to present);
9. PEDro (Physiotherapy Evidence Database) http://www.pedro.org.au/ (1929 to present).
10. Clinicaltrials.gov (www.clinicaltrials.gov);
11. International Clinical Trials Registry Platform (http://apps.who.int/trialsearch/).
12. SPORTDiscus
13. Science Direct

We will adapt the MEDLINE search strategy (Appendix 1) as necessary for each of the other databases. The added study filter is a modified version of the Ovid MEDLINE Cochrane Highly Sensitive Search Strategy for identifying randomised trials (Lefebvre 2011). For EMBASE we will add the study design terms as used by the UK Cochrane Centre (Lefebvre 2011).

Searching other resources

We will screen the reference lists of all relevant articles. We will contact the lead authors of retrieved articles (experts in the field) to identify unpublished data.

Data collection and analysis

Selection of studies

We will conduct the selection of eligible studies in two stages. First, two review authors (GMM, JTC) will independently screen titles and abstracts of the search output, and code each study as 'include' (eligible or potentially eligible/unclear) or 'exclude'. We will exclude all references that clearly do not fulfil our inclusion criteria. At the second stage, we will retrieve the full-text study reports and two review authors (GMM, JTC) will independently screen the full-text and identify studies which meet the inclusion criteria. We will also identify and record reasons for exclusion of the ineligible studies so that we can report these in a 'Characteristics of excluded studies' table. We will resolve any disagreement through discussion or, if required, we will consult a third person (MS, FB, IBS, DB or AJEB). We will identify and exclude duplicates and collate multiple reports of the same study so that each study rather than each report is the unit of interest in the review. We will record the selection process in sufficient detail to complete a PRISMA study flow diagram (Liberati 2009).

Data extraction and management

We will use a data collection form for study characteristics and outcome data, which has been piloted on at least one included study. Two review authors (GMM, JTC) will extract the following characteristics from the included studies.

1. Methods: study design, duration of study, study location, study setting, withdrawals, and date of study.
2. Participants: N, mean age or age range, gender, inclusion criteria, and exclusion criteria.
3. Interventions: description of intervention, comparison, duration, intensity, content of both intervention and control condition, and co-interventions.
4. Outcomes: description of primary and secondary outcomes specified and collected, and at which time points reported.
5. Notes: funding for trial, and notable conflicts of interest of trial authors.

Two review authors (GMM, JTC) will independently extract outcome data from included studies. We will note in the 'Characteristics of included studies' table if outcome data were not reported in a usable way. We will resolve disagreements by consensus or by involving a third person (MS, FB, IBS, DB or AJEB). One review author (GMM) will transfer data into the Review Manager (RevMan 2014) file. We will double-check that data were entered correctly by comparing the data presented in the systematic review with the study reports. A second review author (JTC) will spot-check study characteristics for accuracy against the trial report.

Assessment of risk of bias in included studies

Two review authors (DNB, AJEB) will independently assess risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will resolve any disagreements by discussion or by involving another author (GMM). We will assess the risk of bias according to the following domains.

1. Random sequence generation.
2. Allocation concealment.
3. Blinding of participants and personnel.

4. Blinding of outcome assessment.
5. Incomplete outcome data.
6. Selective outcome reporting.
7. Other bias.

We will grade each potential source of bias as high, low or unclear risk, and provide a quote from the study report together with a justification for our judgment in the 'Risk of bias' table. We will summarise the 'Risk of bias' judgements across different studies for each of the domains listed. We will consider blinding separately for different key outcomes where necessary. Where information on risk of bias relates to unpublished data or correspondence with a trialist, we will note this in the 'Risk of bias' table.

When considering treatment effects, we will take into account the risk of bias for the studies that contribute to that outcome.

Assesment of bias in conducting the systematic review

We will conduct the review according to this published protocol and report any deviations from it in the 'Differences between protocol and review' section of the systematic review.

Measures of treatment effect

We will enter the outcome data for each study into the data tables in RevMan (RevMan 2014) to calculate the treatment effects. We will use mean differences or standardised mean differences for continuous outcomes, or other types of data as reported by the study authors. If only effect estimates and their 95% confidence intervals or standard errors are reported in studies, we will enter these data into RevMan using the generic inverse variance method. We will ensure that higher scores for continuous outcomes have the same meaning for the particular outcome, explain the direction to the reader and report where the directions were reversed if this was necessary. When the results cannot be entered in either way, we will describe them in the 'Characteristics of included studies' table, or enter the data into Additional tables.

Unit of analysis issues

For studies that employ a cluster-randomised design and that report sufficient data to be included in the meta-analysis but do not make an allowance for the design effect, we will calculate the design effect based on a fairly large assumed intra-cluster correlation (ICC) of 0.10. We base this assumption of 0.10 being a realistic estimate by analogy on studies about implementation research (Campbell 2001). We will follow the methods stated in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) for the calculations.

Dealing with missing data

We will contact investigators or study sponsors in order to verify key study characteristics and obtain missing numerical outcome data where possible (e.g. when a study is identified as abstract only). Where this is not possible, and the missing data are thought to introduce serious bias, we will explore the impact of including such studies in the overall assessment of results by a sensitivity analysis.

If numerical outcome data are missing, such as standard deviations or correlation coefficients, and they cannot be obtained from the authors, we will calculate them from other available statistics such as P values according to the methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Assessment of heterogeneity

We will assess the clinical homogeneity of the results of included studies based on similarity of population, intervention, outcome and follow-up. We will consider populations as similar when they are the same professional (e.g. military and mining) or athletic group (e.g. team sports) only, or the entire population of a workplace. We will consider interventions as similar when they fall into the same category as mentioned in Types of interventions above. We will consider the measurement of rectal, aural and oesophageal temperatures as similar and term these as core temperature. We will categorise intervention durations as short-term, medium-term and long-term heat acclimation as described in the Description of the intervention above. We will categorise follow-up times directly post-intervention (within 48 hours after the final intervention session), and acclimation decay intervals every six to seven days for up to four weeks post-intervention as different.

We will use the I^2 statistic to measure heterogeneity among the trials in each analysis. If we identify substantial heterogeneity we will report it and explore possible causes by prespecified subgroup analysis. Values of I^2 will be interpreted as follows: 0% to 40% might not be important; 30% to 60% may represent moderate heterogeneity; 50% to 90% may represent substantial heterogeneity; and 75% to 100% may represent considerable heterogeneity.

Data synthesis

We will pool data from studies judged to be clinically homogeneous using Review Manager 5.3 software (RevMan 2014). If more than one study provides usable data in any single comparison, we will perform a meta-analysis. We will use a random-effects model when I^2 is above 40%; otherwise we will use a fixed-effect model. When I^2 is higher than 75% we will not pool results of studies in meta-analysis.

We will narratively describe skewed data reported as medians and interquartile ranges.

Where multiple trial arms are reported in a single trial, we will include only the relevant arms. If two comparisons are combined

in the same meta-analysis, we will halve the control group to avoid double-counting.

Subgroup analysis and investigation of heterogeneity

Where data allow, we intend to perform the following subgroup analyses:

- Gender (male versus female)
- Physical capacity (e.g. trained versus untrained)
- Exposure dose (e.g. short versus medium versus long exposure durations; active versus passive heat exposure)
- Exercise type (e.g. low intensity versus high intensity exercise; isothermic versus fixed-intensity)

We will use the Chi² test to test for subgroup interactions in Review Manager (RevMan 2014).

Sensitivity analysis

If there is high risk of bias associated with some of the included trials, we will perform sensitivity analysis to determine whether the risk of bias significantly influences the effect size. We will consider trials to be at high risk of bias in sensitivity analysis if allocation concealment is rated as unclear or high risk, or if attrition is greater than 20%. We will also carry out sensitivity analysis to explore the effects of fixed-effect or random-effects analyses for outcomes with statistical heterogeneity and the effects of any assumptions made, such as the value of the ICC used for cluster-randomised trials. If any study at high risk of bias significantly influences the effect size, these studies will be excluded from the meta-analysis but will be reported in narrative form.

'Summary of findings' table

We will create a 'Summary of findings' table using all outcomes listed under Types of outcome measures. We will use the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of a body of evidence as it relates to the studies which contribute data to the meta-analyses for the prespecified outcomes. We will use methods and recommendations described in Section 8.5 and Chapter 12 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) using GRADEpro software (GRADEproGDT 2015). We will justify all decisions to down- or up-grade the quality of studies using footnotes.
We will also compile an additional GRADE table showing all of our decisions about the quality of evidence and their justifications.

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* *Indicates the major publication for the study*

APPENDICES

Appendix 1. MEDLINE search strategy

Ovid MEDLINE(R), Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid OLDMEDLINE(R)

1. heat stress disorders/ or heat exhaustion/ or heat stroke/
2. Dehydration/
3. Sweat/
4. Hot Temperature/ae [Adverse Effects]
5. (heat adj3 stress).ab,ti.
6. "sweat*".ab,ti.
7. ((hot or warm or humid) adj3 (condition* or temperature*)).ab,ti.
8. (humidity or heat).ab,ti.
9. adverse effects.fs.
10. 8 and 9
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 10
12. adaptation, physiological/ or acclimatization/
13. body temperature regulation/ or skin temperature/
14. exercise/ or physical conditioning, human/ or resistance training/ or running/ or swimming/ or walking/ or warm-up exercise/
15. (walk* or run* or jog* or exercise* or swim* or warm-up or stretch* or work-out or physical).ab,ti.
16. (heat adj3 acclimation).ab,ti.
17. Acclimatization.ab,ti.
18. acclimation program*.ab,ti.
19. (acclimation and (long or short or hot or humid)).ab,ti.
20. "acclimation temperature".ab,ti.
21. 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20
22. randomi?ed.ab,ti.
23. randomized controlled trial.pt.
24. controlled clinical trial.pt.
25. placebo.ab.

26. clinical trials as topic.sh.
27. randomly.ab.
28. trial.ti.
29. Comparative Study/
30. 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29
31. (animals not (humans and animals)).sh.
32. 30 not 31
33. 11 and 21 and 32

CONTRIBUTIONS OF AUTHORS

GMM led the writing of the protocol. GMM is guarantor of the protocol.

MS commented on different versions of the protocol and approved the final protocol.

FB commented on different versions of the protocol and approved the final protocol.

IBS commented on different versions of the protocol and approved the final protocol.

DNB commented on different versions of the protocol and approved the final protocol.

AJEB commented on different versions of the protocol and approved the final protocol.

JTC commented on different versions of the protocol and approved the final protocol.

DECLARATIONS OF INTEREST

Geoffrey Minett: None known.

Melissa Skein: None known.

Francois Bieuzen: None known.

Ian Stewart: Heat strain evaluation of security officers wearing personal body armour for Chubb Security Services. Expert witness in heat stress management trial for security guards wearing personal body armour for Chubb Security Services. Grant received for heat strain evaluation of EOD & CBRN personal protective clothing from Defence Science and Technology Organisation & US Combatting Terrorism Technical Support Office.

David Borg: None known.

Aaron Bach: None known.

Joseph Costello: None known.