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COLD WATER IMMERSION: KILL OR CURE?

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New Findings

This is the first review to look across the broad field of "cold water immersion" and to determine the threat and benefits associated with it as both a hazard and a treatment. The level of evidence supporting each of the areas reviewed is assessed.

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Abstract

Like other environmental constituents such as pressure, heat and oxygen, cold water can be either good or bad, threat or treatment depending on circumstance. Given the current increase in the popularly of open cold water swimming it is timely to review the various human responses to cold water immersion (CWI) and consider the strength of the claims made for the effects of CWI. As a consequence, in this review we look at the history of CWI and examine CWI as a pre-cursor to drowning, cardiac arrest and hypothermia. We also assess its role in prolonged survival underwater, extending exercise time in the heat and treating hyperthermic casualties. More recent uses, such as in the prevention of inflammation and treatment of inflammation-related conditions are also considered. It is concluded that the evidence-base for the different claims made for CWI are varied, and whilst in most cases there seems to be a credible rationale for the benefits or otherwise of CWI, in some cases the supporting data remain at the level of anecdotal speculation. Clear directions and requirements for future research are indicated by this review.

Introduction: History

For centuries cold water has been regarded as both “hero” and “villain”, as having both beneficial and detrimental effects. In 450 BC Herodotus (450 BC) describing the ill-fated seaborne expedition of the Persian General Mardonius wrote, “..those who could not swim perished from that cause, others from the cold”. In December 1790 Dr James Currie, a physician, stood with a crowd unable to help as the crew of a stranded American sailing ship fell into the 5 °C sea and drowned. This experience led Currie to undertake the first recorded experiments on the effects of cold water immersion (CWI) on humans.

Claims for the health benefits of cool and CWI, spa or sea, also date back centuries. According to Hippocrates, water therapy allayed lassitude, and Thomas Jefferson used a cold foot bath every morning for six decades to “maintain his good health”. Largely anecdotal evidence extols the virtues of CWI or cold water swimming as a means of improving well-being and health (Digby 1587, cited in Parr, 2011). These health benefits are believed to be a consequence of the physiological responses

and biochemical milieu which occurs from exposure to cold water (Huttunen *et al*. 2004, Kukkonen-Harjula & Kauppinen, 2006). The changes occur acutely during CWI, with repeated bouts of CWI resulting in adaptive responses that may also impact upon indices of health.

In the middle ages people did not learn to swim because they would then not be able to cross the river Styx when condemned to enter hell. 1539, Wynmann wrote the first swimming book in an attempt to introduce a "human stroke" and thereby reduce the number of drownings. As early as 1750 published work recommended sea swimming (and sea water drinking!) for the treatment of a range of diseases (Russell, 1755; Buchan, 1769), with winter considered the best time to engage in the activity. Sea bathing reached a peak in popularity in the late eighteenth century around the time of the development of the "swim suit" and "bathing machine". Whole communities, seaside resorts, were founded on the perceived health benefits of sea swimming. The hazard associated with this health benefit led to the introduction of beach lifeguarding (Tipton & Wooler, 2016). The modern age of open water swimming, as opposed to bathing, probably began on the 3rd May 1810 when Lord Byron swam several miles across the Dardanelles (Hellespont) from Europe to Asia.

INSERT FIGURE 1 ABOUT HERE

Recently there has been a significant growth in the number of people engaging in open, cold water swimming, both in terms of competitions (ice swimming, marathon swimming, winter swimming and triathlon) and general "wild swimming". With increased participation has come renewed and enthusiastic claims for the physiological and psychological health benefits associated with CWI. It therefore seems timely to review the evidence for the hazards and benefits associated with the stress of CWI.

Cold Water: Hazards

In 2012 an estimated 372,000 people (42 per hour) died from immersion, assumed to be drowning. Immersion is the third leading cause of unintentional injury-related death, accounting for 7 % of all such deaths (WHO, 2014). These figures are under-estimations due to poor reporting in many Third World countries that have a high number of deaths. The data also do not include life-long morbidity caused by immersion-related injuries, estimated to be a much bigger numerical problem.

There is no strict definition of "cold water". Given that some of the hazardous responses to cold water appear to peak on immersion somewhere between 15 °C and 10 °C it is reasonable to say that

cold water is water below 15 °C (Tipton *et al.* 1991). However, thermoneutral water temperature for a resting naked individual is about 35 °C so it is possible for individuals to become very cold, with time, on immersion in water below this temperature. The corresponding temperatures for those exercising (including shivering) is about 25 °C (Tipton & Golden, 1998).

Historically, the threat associated with CWI was regarded in terms of hypothermia or a fall in deep body temperature below 35 °C. This belief was established as a result of the Titanic disaster and supported by data obtained during maritime conflicts of WWII. However, more recently a significant body of statistical, anecdotal and experimental evidence has pointed towards other causes of death on immersion. For example, in 1977 a Home Office Report revealed that approximately 55 % of the annual open-water deaths in the UK occurred within 3 m of a safe refuge (42 % within 2 m), and two thirds of those that died were regarded as "good swimmers". This evidence suggests more rapid incapacitation than can occur with whole body cooling and consequent hypothermia.

Four stages of immersion have been associated with particular risks (Golden & Hervey, 1981; Golden *et al.* 1991), the duration of these stages and the magnitude of the responses evoked within them vary significantly; depending on several factors, not least of which water temperature:

- Initial immersion (first 3 minutes): skin cooling
- Short-term immersion (3 min plus): superficial neuromuscular cooling
- Long-term immersion (30 min plus): deep tissue cooling (hypothermia)
- Circum-rescue collapse: just before, during or soon after rescue

As a result of laboratory-based research, the initial responses to immersion, or "cold shock", were identified as particularly hazardous (Tipton, 1989), accounting for the majority of immersion deaths (Tipton *et al.* 2014). These deaths have most often been ascribed to drowning, with the physiological responses of a gasp and uncontrollable hyperventilation, initiated by the dynamic response of the cutaneous cold receptors, resulting in the aspiration of the small volume of water necessary to initiate the drowning process (Bierens *et al.* 2016). Relatively little is known about the minimum rates of change of cold receptor temperature necessary to cause cold shock. The response has been reported to begin in water as warm as 25 °C but is easily consciously suppressed at that temperature. Under laboratory conditions, the respiratory frequency response (an indication of respiratory drive) peaks on naked immersion in a water temperature between 15 and 10 °C, getting no greater on immersion in water at 5 °C (Tipton *et al.* 1991). The corresponding average rates of

change of chest skin temperature over the first 20 seconds of these immersions was 0.42 °C.s^{-1} (Tw 15 °C); 0.56 °C.s^{-1} (Tw 10 °C) and 0.68 °C.s^{-1} (Tw 5 °C). This suggests that an average rate of change in chest skin temperature between 0.42 – 0.56 °C.s^{-1} on the first 20 seconds of immersion is sufficient to evoke a maximum respiratory cold shock response.

More recently it has been suggested (Shattock & Tipton, 2012) that a larger number of deaths than once thought may be due to arrhythmias initiated on immersion by the coincidental activation of the sympathetic and parasympathetic division of the autonomic nervous system by stimulation of cutaneous cold receptors around the body (sympathetic activation [cold shock]) and in the oronasal region on submersion or with wave splash (vagal stimulation [diving response]). This "Autonomic Conflict" is a very effective way of producing dysrhythmias and arrhythmias even in otherwise young and healthy individuals, particularly, but not necessarily, if a prolonged breath hold is involved in the immersion (Tipton *et al.* 1994). It seems predisposing factors such as long QT syndrome, ischaemia heart disease or myocardial hypertrophy are necessary for fatal arrhythmias to evolve (Shattock & Tipton, 2012); many of these factors, including drug-induced LQTS, are acquired. Non-fatal arrhythmias could still indirectly lead to death if they cause incapacitation and thereby drowning (Tipton, 2013). The hazardous responses associated with the cold shock response are presented in Figure 2.

INSERT FIGURE 2 ABOUT HERE

The problems encountered in short-term immersions are primarily related to physical incapacitation caused by neuromuscular cooling (Castellani & Tipton, 2015). The arms are particularly susceptible due to their high surface area to mass ratio. Low muscle temperatures affect chemical and physical processes at the cellular level. This includes metabolic rate, enzymatic activity, calcium and acetylcholine release and diffusion rate, as well as the series elastic components of connective tissues (Vincent & Tipton, 1988). Maximum dynamic strength, power output, jumping and sprinting performance are related to muscle temperature with reductions ranging from 4-6% per degree Celsius fall in muscle temperature down to 30 °C (Bergh & Ekblom, 1979). At nerve temperatures below about 20°C, nerve conduction is slowed and action potential amplitude is decreased (Douglas & Malcolm, 1955). Nerve block may occur after exposure to a local temperature of between 5 and 15°C for 1 to 15 minutes. This can lead to dysfunction that is equivalent to peripheral paralysis and can, again, result in drowning due to the inability to keep the airway clear of the water (Basbaum, 1973; Clarke *et al.* 1958; Golden & Tipton, 2002. Figure 3).

Even in ice-cold water, the possibility of hypothermia does not arise for at least 30 minutes in adults. Hypothermia affects cellular metabolism, blood flow and neural function. In severe hypothermia, the patient will be deeply unconscious. The progressive signs and symptoms (approximate deep body temperature) are shivering (36 °C), confusion, disorientation, introversion (35 °C), amnesia (34°C), cardiac arrhythmias (33 °C), clouding of consciousness (33-30 °C), loss of consciousness (30 °C), ventricular fibrillation (28 °C), and death (25 °C) (Bierens *et al.* 2016). There is great variability between deep body temperature and the signs and symptoms of hypothermia. For example, although the deep body temperature associated with death is often quoted as 25 °C, the lowest temperature recorded to date following accidental exposure to cold (air) and with full recovery was 12.7 °C in a 28-month-old child (Associated Press, 2015). The coldest adult survivor of CWI followed by submersion had a body temperature of 13.7 °C (Gilbert *et al.* 2000). There is also a large amount of variation in the rate at which people cool on immersion in cold water, due to a combination of thermal factors (including water temperature and water movement, internal and external insulation) and non-thermal factors (including body size and composition, blood glucose, motion illness, racial and sex differences) (Haight & Keatinge, 1973; Gale *et al.* 1981; White *et al.* 1992; Mekjavic *et al.* 2001; Golden & Tipton, 2002).

The most significant practical consequence of hypothermia in water is loss of consciousness; this prevents individuals from undertaking physical activity to maintain a clear airway and avoid drowning. Thus, once again, drowning is often the end-point (Figure 3).

INSERT FIGURE 3 ABOUT HERE

About 17% of those that die as a result of immersion die just before, during or just after rescue (Golden *et al.* 1991). The deaths just before rescue are intriguing and probably related to behavioural changes at this time or the relief and psychophysiological alterations associated with imminent rescue, including a reduction in circulating stress hormone concentration and an increase in vagal tone. Death during rescue is most commonly associated with a collapse in arterial pressure when lifted vertical from the water and kept in that position for some time (Golden *et al.* 1991).

Finally in this section it is worth mentioning that because sea water freezes at -1.9 °C and human tissue at -0.55 °C it is possible to get frostbite in the sea, although this is a rare occurrence. Much more common, but less well known and understood, is non-freezing cold injury (NFCI). This can be

caused by short immersions in very cold water or longer duration immersions in cool water. In reality the details of the pathogenesis and pathology of NFCI are not fully understood but the consequences: cold sensitivity; hyperhidrosis; and intractable pain, can be debilitating and permanent (Golden *et al.* 2013; Heil *et al.* 2016). Those advocating very cold water immersion, for example post-exercise, are often unaware of this risk.

Cold Water: Benefits

a. Prolonged survival under water

Generally, drowning results in cardiopulmonary arrest within two minutes (Fainer *et al.* 1951). Quan *et al.* (2014) reported on the outcome of 1,094 open water drownings: most (78 %) had bad outcomes (74 % death, 4 % severe neurological sequelae), of the good outcomes, 88 % were submerged for less than 6 minutes. This percentage falls rapidly (i.e. 7.4 % of good outcomes when submerged 6-10 minutes), with the risk of death or severe neurological impairment after hospital discharge given as "nearly 100 %" when the duration of submersion exceeds 25-27 minutes (Szpilman *et al.* 2012).

However, if the water is cold this time can be extended, with the current "record" being 66 minutes of submersion with near-complete recovery (Bolte *et al.* 1988). In such cases the temperature of the water appears protective, with recorded submerged survival with minimal long term sequelae only having been reported in water below 6 °C (Tipton & Golden, 2011). The Q_{10} temperature coefficient, a measure of the rate of change of a biological or chemical system as a consequence of increasing/decreasing the temperature by 10 °C, differs for different body systems: metabolic and rhythmic processes are particularly depressed by hypothermia (Q_{10} of about 3); contractile processes have a Q_{10} of about 2. As hypothermia progresses metabolic and rhythmic processes are depressed more than the rates of diffusion of different metabolites (MacLean & Emslie-Smith, 1977). The hypoxic survival time of the brain is extended by hypothermia, with cerebral activity and therefore oxygen demand, falling close to minimal levels at a brain temperature of 22 °C (Adams & Victor, 1977).

The proposed mechanism of prolonged underwater survival involves the two minutes of drowning-related flushing of cold water in and out of the lung cooling the heart and carotid artery blood supply to the brain, thereby *selectively* cooling the brain, with consequent cerebral hypothermia protecting the brain from hypoxia (Golden *et al.* 1997; Tipton & Golden, 2011). Evidence for such a mechanism can be found in the animal work of Conn *et al.* (1995) who reported a 7.5 - 8.5 °C fall in carotid artery

temperature after two minutes of submersion, with much slower cooling (0.8 °C) during head out cooling. The cooling rate also slows significantly after cardio-respiratory arrest (Conn *et al.* 1995), further supporting the involvement of respiratory heat exchange in the initial fast rates of cooling of carotid artery temperature. Although slower, continued cooling via surface cooling does add important additional protection; this helps explain why those that cool the most by this route due to surface area:mass ratio advantages (i.e. the young and the small) tend to comprise the small number of individuals who have survived prolonged immersion with minimal consequences. Because the brain is preferentially cooled, other sites for measuring deep body temperature have little prognostic value in such situations (Golden & Tipton, 2011).

Therefore, in contrast to the problems caused by cold shock outlined in the previous section, in this scenario (small individual submerged in water <6 °C) the hyperventilation associated with cold shock during drowning may be beneficial rather than detrimental; this highlights the importance of circumstance for making such conclusions. Interestingly, the same protective mechanism that can occur naturally during drowning in very cold water has been considered as an intervention to reduce ischaemic brain damage following cardiac arrest or stroke. The challenge is to find a method that can cool the brain rapidly enough to be of value (Hoa *et al.* 2008; Rewell *et al.* 2017).

b. Deliberate cooling

i. Cooling for hyperthermia and heat illness

Cooling strategies are used by athletes to cool themselves between bouts of exercise, such interventions are also used to treat those with heat illness ranging from heat exhaustion to potentially fatal heat stroke.

Various techniques, including ice-vests, air and water-perfused vests, have been developed to cool individuals between and following bouts of exercise. Of these, hand immersion in cold water and whole body fanning with or without artificial sweating (water spraying) have been shown to be preferential when a viable peripheral circulation remains (Barwood *et al.* 2009). This is because these techniques use the physiology of the body to deliver heat to the skin via the circulation rather than try and overwhelm it and remove heat via conduction. The latter approach runs the risk of evoking the body's heat loss defence mechanisms, including vasoconstriction, thereby resulting in slower cooling. The same mechanisms explain why whole body immersion in temperate water (26 °C) is as effective at removing heat from a resting body as immersion in cold water (14 °C) when there is a viable circulation (Tipton, 2006; Taylor *et al.* 2008; Casa *et al.* 2010). However, in absence

of a viable circulation, such as in heat stroke, heat loss by conduction remains the only available route and therefore in such circumstances heat loss is inversely related to water temperature (Proulx *et al.* 2003; Zang *et al.* 2015).

ii. Pre-cooling for performance

It has long been known that prolonged exercise performance is diminished in hot environments compared to cooler conditions (Galloway & Maughan, 1997; Tatterson *et al.* 2000). The mechanisms thought to underpin the ergolytic effect of heat are complex and varied but are, broadly speaking, due to the direct and indirect consequences of hyperthermia on body temperatures (e.g. brain) and regional (e.g. muscle/skin) blood flows (Cheuvront *et al.* 2010; Febbraio, 2000; Nielsen & Nybo, 2003; Nybo, 2008). Any intervention which creates a heat sink by reducing the initial body heat content (pre-cooling) should enable the storage of a greater amount of heat before reaching a given level of hyperthermia. Thus, pre-cooling might potentially be ergogenic during exercise in a hot environment. Equally, pre-cooling may be debilitating if sufficient to impair neuromuscular function (see earlier section). Its will therefore depend on the nature of the cooling stimulus (muscle cooling *vs.* deep body cooling) and the event (power output *vs.* endurance) to be undertaken as well as environmental conditions.

Perhaps the first study examining the effect of pre-cooling on tolerance to hot conditions was conducted by Veghte & Webb (1961) who used different durations of CWI (16 °C), as well as air cooling, to demonstrate that the resting tolerance time in a high ambient temperature (71 °C) was inversely related to the initial body temperature. The first pre-cooling studies examining exercise performance typically used pre-exercise cold air exposure, rather than CWI, and investigated performance under relatively temperate environmental conditions (T_{db} 18-24 °C). Nevertheless, these studies demonstrated that reducing initial body-heat content resulted in reduced thermophysiological strain and improved exercise performance (Schmidt & Brück, 1981; Hessemer *et al.* 1984; Olschewski & Bruck, 1988; Lee & Haymes, 1995), although the combination of sub-optimal convective cooling and relatively high metabolic rates in these studies would likely have induced a potentially limiting thermal-burden, even under these relatively benign ambient conditions (Ely *et al.* 2007). However, because the thermal conductivity of water is 24× that of air, and the energy required to heat a given volume of water by 1 °C is 3500× that of air, the cooling power of cold water in terms of human deep body temperature is approximately three times that of cold air at the same temperature (Smith & Hanna, 1975). Consequently, a given rate of heat loss can be achieved at a higher temperature, and with a narrower skin-environment temperature gradient

in water, than in air (Marino, 2002). Indeed, there is evidence from meta-analysis that CWI is more effective than all other types of pre-cooling intervention (Jones *et al.* 2012)

Perhaps the seminal study examining the effectiveness of pre-exercise CWI on exercise performance in the heat is that of Booth *et al.* (1997), using a counterbalanced design they got eight trained participants (average $\dot{V}O_{2max}$ = 63.1 mL·kg·$^{-1}$min^{-1}) to undertake a 30 minute run in hot-humid conditions (32 °C, 60 % RH) on two occasions: with, or without (control), prior CWI. The CWI consisted of 60 minutes of immersion in water which, to minimise discomfort, was progressively cooled from ~29 °C to ~23 °C. This reduced the pre-exercise rectal temperature (T_{re}), mean skin temperature ($\bar{T}_{sk}$) and heart rate by ~0.7 °C, 5.9 °C and 13 %, respectively. The reduced T_{re}, $\bar{T}_{sk}$ and heart rate persisted for 20, 25 and 10 minutes respectively during the exercise bout and enabled the participants to run significantly further than in the control condition (average 304 m). A similarly influential study was undertaken by González-Alonso *et al*. (1999) in which participants undergoing 30 minutes of CWI at 17 °C, had an initial average oesophageal temperature (T_{oes}) of 35.9 °C and were subsequently able to cycle for 63 minutes at 60 % $\dot{V}O_{2max}$ in a hot environment (40 °C, 19 % RH), whereas immersion in 36°C water resulted in an initial T_{oes} of 37.4 °C and an average time to exhaustion of 46 minutes. Following warm water immersion (40 °C) a starting T_{oes} of 38.2 °C and time to exhaustion of 28 minutes were recorded. Numerous subsequent studies have confirmed the efficacy of pre-cooling by CWI (*e.g.* Duffield *et al.* 2010; Siegel *et al.* 2012; Skein *et al.* 2012).

However it should be noted that, in accordance with Newton's cooling Law (Newton, 1700) and the heat transfer equation (Fourier,1807), in a hot environment pre-cooling increases the rate of heat transfer between the human body and the environment as a consequence of an increased thermal gradient (Taylor *et al.* 2014). The onset of sweating is also delayed during exercise after pre-cooling (Wilson *et al*. 2002), which will diminish evaporative heat loss. As a result a pre-cooled individual will gain heat more rapidly than a hotter individual until convergence at a common temperature (Booth *et al.* 2004). Thus, whilst pre-cooling by CWI represents an effective strategy for enhancing endurance exercise performance in a hot environment, its efficacy may be limited to exercise durations shorter than the time taken for body temperature to converge with that in a non-pre-cooled condition.

iii. Post-exercise CWI for recovery

The use of CWI following intense exercise is prevalent among sports people and primarily stems from the belief that CWI facilitates aspects of recovery and regeneration, thereby conferring a

potential training and performance advantage (Versey *et al.* 2013; Leeder *et al.* 2015). The potential negative aspects of post-exercise immersion in ice-cold water, such as non-freezing cold injury (see earlier section), often do not seem to be considered.

The physiological mechanisms by which post-exercise CWI influences recovery are not entirely clear (White & Wells, 2013), but are most likely related to effects of removal of body heat, reduced tissue temperature and hydrostatic pressure effects, rather than to the cold shock response (Figure 4). For example, decreased tissue temperature may reduce acetylcholine production, lower nerve conduction velocity (Abramson *et al*. 1966) and firing rate of the muscle spindles (Ottoson, 1965). These alterations could decrease muscle spasm and exert an analgesic effect (Meeusen & Lievens, 1986; Wilcock *et al*. 2006). Alternatively, hydrostatic pressure might reduce oedema and inflammation by increasing the pressure gradient between the interstitial and intravascular space, promoting the re-absorption of interstitial fluid in a manner similar to compression stockings (Partsch *et al.* 2004). Cold and hydrostatic pressure could also act synergistically: decreased muscle temperature may reduce oedema by reducing muscle perfusion (cold-induced vasoconstriction) and fluid diffusion into the interstitial space (Yanagisawa *et al.* 2010; Gregson *et al.* 2011), as well as through reduced permeability of the cellular, lymphatic and capillary vessels (Coté *et al.* 1988). This might complement any hydrostatic pressure effects on interstitial-intravascular fluid movement.

Regardless of the underlying mechanism, reduced oedema is hypothesised to better preserve the oxygen supply to cells; this supply may otherwise become compromised by local swelling and the associated capillary constriction (Wilcock *et al.* 2006), although the extent to which this offset by the decreased perfusion is unclear. Additionally, a decreased tissue temperature should, as noted above, reduce the metabolic rate and oxygen requirement of the cooled tissue (Drinkwater, 2008). Together these effects could lessen exercise-induced inflammation by decreasing hypoxic cell death or damage and, by reducing the infiltration of leukocytes and monocytes, minimise secondary tissue damage (Swenson *et al.* 1996; Wilcock *et al.* 2006). Similar claims have been made for hyperbaric oxygen therapy (Kindwall, 1995).

INSERT FIGURE 4 ABOUT HERE

Given these potential benefits it is unsurprising that the use of CWI for facilitating recovery has received considerable attention within the literature. Indeed, a wide variety of protocols have been investigated, with variations in terms of the exercise 'insult', the timing of immersion after exercise,

the temperature, duration and depth of immersion and the outcome measure reported. Thus, given the potential mechanisms of action it is perhaps not unexpected that there is variation in the reported efficacy of CWI among the literature (White & Wells, 2013), with some studies supporting the efficacy of CWI for recovery (*e.g.* Bailey *et al.* 2007; Vaile *et al.* 2008; Ingram *et al.* 2009) and others showing no benefit (*e.g.* Goodall & Howatson, 2008; Corbett *et al.* 2012; Leeder *et al.* 2015). Nevertheless, meta-analyses (Leeder *et al.* 2012; Machado *et al.* 2016) and a Cochrane systematic review (Bleakley *et al.* 2012) of the relevant studies have concluded that CWI is effective at reducing perceived post-exercise muscle soreness, with some meta-analytic evidence also supporting the effectiveness of CWI on reducing blood creatine kinase levels and improving the recovery of muscle power (Leeder *et al.* 2012). However, this assertion should be tempered by the fact that, given the nature of the intervention, it is difficult to administer a true placebo in these studies. In one study that did include a placebo treatment, the effect of CWI was found to be no bigger than the placebo effect (Broatch *et al.* 2014).

It seems reasonable that the control condition for such studies should be the widely used active recovery rather than nothing (rest). Indeed, recent research has reported that infiltration of inflammatory cells, mRNA expression of pro-inflammatory cytokines and neurotrophins, and the subcellular translocation of heat shock proteins did not differ significantly between CWI and active recovery groups following a single bout of resistance exercise. This suggests that CWI is no more effective than active recovery for reducing inflammation or cellular stress in this single-bout exercise model (Peake *et al.* 2017).

Finally, if CWI reduces the inflammatory response to exercise-induced trauma, and this response is important for beneficial adaptations to repeated exercise bouts *i.e.* training, then CWI may actually be counter-productive (Schoenfeld, 2012). Indeed, recent evidence indicates that CWI during a 12 week training programme attenuated long term gains in muscle mass and strength and blunted the activation of key proteins and satellite cells in skeletal muscle up to two days after resistance exercise (Roberts *et al.* 2015). However, CWI may enhance other aspects of the adaptive response to exercise. Ihsan *et al*. (2014) have shown that a 15 minute leg immersion in 10°C water after a single exercise bout consisting of 30 minutes sub-maximal running followed by intermittent running to exhaustion enhances the gene expression of peroxisome proliferator-activated receptor gamma coactivator-1α (PGC-1α), a key regulator of mitochondrial biogenesis, and vascular and metabolic adaptations to exercise. Allan et al. (2017) have presented similar evidence for increased PGC-1α expression with leg CWI, but also demonstrated increased PGC-1α in the non-immersed leg (relative

to a control condition), suggesting that this is a systemic response to CWI, possibly as a consequence of β-adrenergic activation of AMPK.

Importantly, these effects do not appear confined to a single bout of exercise and CWI with Ihsan *et al*. (2015) demonstrating that some (*e.g.* p38 MAPK, AMPK, and mitochondrial proteins complex I, complex III, and β-HAD), although not all, indices of mitochondrial biogenesis were increased when individuals underwent post-exercise CWI following 3 sessions·wk^{-1} of endurance training for 4 weeks. However, the physiological significance of these finding remains unclear with Yamane *et al*. (2006) reporting attenuated improvements in maximal oxygen uptake when CWI was used after training in a 4 week endurance training programme consisting of 3-4 training sessions·week^{-1}; it has been suggested that CWI may dissociate the relationship between mitochondrial content and exercise performance and the increase in mitochondrial content could be offset by increased uncoupled mitochondrial respiration (Ihsan *et al*., 2015). More work is required to elucidate these potentially conflicting responses as well as establish the cold stimulus/dose (intensity, duration and number of exposures) required to produce them.

c. Inflammation

Keeping with the topic of inflammation, there is an expanding body of evidence linking inflammation with health and disease. It has been shown that centenarians and supercentenarians have lower levels of inflammation than community-living very old (85 to 99years) people (Arai *et al.* 2015). This study also showed that while centenarians and their offspring were able to maintain long telomeres, telomere length was not a predictor of successful ageing whereas a low inflammation score was. Inflammation has also been associated with conditions including atrial fibrillation (AF) (Boos *et al*. 2006, Dernellis *et al*. 2004), atherosclerosis (Hansson, 2005), inflammatory bowel disease (Kaser *et al.* 2010), type 2 diabetes (Donath & Shoelson 2011), Alzheimer's (Wyss-Coray, 2006) and depression (Miller & Raison 2016).

Modification of the inflammatory response has been associated with improved outcomes in both AF (Dernellis *et al*. 2004) and depression (Muller *et al*. 2006). Cold water habituation has also been shown to improve insulin sensitivity (Hanssen *et al.* 2015). Whether or not the two are linked habituation, especially when part of an exercise programme, is recognised as a therapeutic intervention for type 2 diabetes (Sigal *et al.* 2006; Boulé *et al.* 2001).

As noted, historical documents and anecdotal evidence extol the virtues of CWI or cold water swimming as a means of improving well-being and health (Digby 1587, cited in Parr, 2011). These health benefits are believed to be a consequence of the physiological responses to CWI and, particularly, alterations in these responses with cold water adaptation (Huttunen *et al*. 2004, Kukkonen *et al.* 2006). However, while controlled trials into the therapeutic use of CWI are lacking, there is a theoretical, physiological basis suggesting that this is an area worthy of investigation (Shevchuk 2008; Harper 2012).

The aim of any therapeutic intervention should be to reduce the magnitude of pro- inflammatory triggers and cold water adaptation, developed through repeated immersions, may offer such a model. The hypothesis is that cross-adaptation exists between CWI and other forms of physiological stress such as surgery or inflammatory- based conditions. By reducing the magnitude of the stress response, some of the negative consequences of this may be reduced or avoided. Anecdotal evidence also exists of therapeutic benefit from cold water adaptation for conditions associated with chronically elevated levels of inflammation (Starr, 2013; Harper, 2012; Waters, 2016).

The stress and inflammatory responses of adapted cold water swimmers were found to be lower than unadapted volunteers. For example, resting plasma noradrenaline concentrations were either similar or declined in adapted swimmers (Leppäluoto *et al*., 2008, Hirvonen *et al*. 2002). Catecholamine concentrations were elevated from baseline by two to three-fold during CWI in those that are cold habituated (Leppäluoto *et al*., 2008), but these increases were less than those observed in unadapted individuals (Goldstein & Frank, 2001; Leppäluoto *et al*. 2008). Additionally, repeated CWI reduce plasma adrenocorticotrophic hormone and cortisol responses to CWI (Leppäluoto *et al*. 2008, Huttunen *et al.* 2000). Whilst the cytokine responses to repeated CWI shows no change in resting TNF-α, IL-6 and IL-1β in volunteers, provocation by lipopolysaccharide stimulation results in reduced IL-6 following repeated CWI (Dugué & Leppänen, 2000). However, the cytokine response must be treated with caution as the inflammatory response is complicated and low values are measured prior to cold water adaptation. It remains to be determined what effect cold water adaptation has on cytokine responses in patients with raised levels of inflammatory markers.

Following CWI and cold-pressor tests, increased concentrations of dopamine (Šrámek *et al.* 2000), serotonin, (Hirvonen *et al.* 2002) and beta-endorphins (Suzuki *et al.* 2007) have been reported; these changes are associated with improved mood or the 'post swim high' (Steinberg & Sykes, 1985). However, in contrast to the sympathoadrenal response, the levels of these chemicals have not been reported to change following cold water adaptation (Hirvonen *et al.* 2002). Pro-inflammatory

cytokine release inhibits serotonin production and can promote behaviour change, including initiation of depressive symptoms such as sadness, fatigue and social withdrawal (Slavich & Iwrin, 2014). For example, the release of the pro-inflammatory cytokine Indoleamine 2, 3-dioxygenase (IDO) degrades tryptophan, a pre-cursor to serotonin, and competes with the serotonin metabolic pathway. As a consequence serotonin availability is reduced (Muller & Schwarz, 2007), a change that is thought to contribute to the development of symptoms of depression (Almond, 2013). This mechanism has also been found in rats displaying depression-like symptoms, swim training of the rats inhibited activation of IDO and reduced the depression-like symptoms (Liu *et al.* 2013). Consequently, it has been suggested that adaptation to CWI could reduce pro-inflammatory responses in humans, enhancing serotonin secretion and reducing symptoms of inflammatory-based depressive disorders (Figure 5). It is not clear if this pathway is specific for depressive disorders or if it could potentially ameliorate other inflammatory-based conditions.

INSERT FIGURE 5 ABOUT HERE

Teleologically it makes sense for there to be, at least in part, a common or shared physiological pathway in the response to stress. However, even having established a theoretical basis for the effect of cold water adaptation on the inflammatory response, it is still necessary to demonstrate that adaptation in one system is reflected in another. Repeated exposure to a stressor evokes specific adaptive responses (Adolph, 1956), but there is also a component of general adaptation, often involving the autonomic nervous system, that is common to several stressors (Seyle, 1950; Lunt *et al.* 2010).

Such “cross-adaptation” was shown by Lunt *et al.* (2010) when they demonstrated that habituation of the sympathetic nervous response to short-term CWI (six, five-minute immersions in 12 °C stirred water) also improved the response to moderate exercise in hypoxic conditions (F_IO_2 0.12). Repeated CWI has been reported to increase the concentration of antioxidants in winter swimmers (Siems *et al.* 1999). Specific cold shock proteins have been identified in mammalian cells (Fujita, 1999) and cold exposure increases the expression of heat shock proteins (Holland *et al.* 1993; Lindquist *et al.* 2014). Thus, cold adaptation could enhance tolerance to other forms of stress by up-regulating cell protective mechanisms. This suggests that at the cellular level there may be a *generalised* response to different forms of stress, it is these general responses which may allow, once habituated, a reduction in the response to a novel stressor, if that novel stressor shares the same general responses. Thus, through cross adaptation or cross tolerance, it may be possible to find common

adaptive responses which occur with repeated CWI (Figure 5), that also reduce biochemical markers causing or contributing to ill-health. The combination of the neurotransmitter and anti-inflammatory responses to repeated CWI may be the cross-adaptive link.

Whilst cross-adaptation is probably the key to the therapeutic effectiveness of cold water adaptation, there are other mechanisms which may be employed to further enhance the effect. Cold water adaptation studies typically utilise a set, static immersion protocol; it is more likely that in real-life, cold water swimming will be the preferred technique. This would then be expected to provide the additional health benefits that are derived from exercise (Liu *et al.* 2013, MacAuley *et al*. 2015). In addition open water swimming is thought to offer a range of other potentially beneficial 'interventions' including "green therapy" (Gilbert, 2016) and "blue therapy" (Nutsford *et al*. 2016) as well as the communal aspects and a sense of achievement (Waters, 2016). Green therapy and blue therapy involves access to and use of outdoor, green and blue spaces; green spaces are open land which are primarily vegetation, and blue spaces are bodies of water such as lakes, rivers or the sea. Of particular note is the powerful parasympathetic stimulation derived from immersing the face in cold water (de Burgh Daly & Angell-James, 1979). Studies using electrical stimulation of the vagus nerve have been shown to have significant anti- inflammatory effects (Bonaz *et al*. 2016). Vagal nerve stimulation was approved by the Food and Drug Administration in the US for the treatment of drug-resistant epilepsy and depression in 1997 and 2005 respectively. Since then, 80,000 patients with epilepsy and 4000 with depression have had bipolar pulse generators connected to electrodes wrapped around the left VN in the neck implanted, with encouraging results (Englot *et al.* 2011; Bonaz *et al* 2016). Cold immersion of the face might represent a safer and cheaper means of stimulating the vagus?

At present, research does not unequivocally support the use of cold water adaptation (indoors or outdoors, static or swimming) for therapeutic purposes. There is a theoretical basis as well as non-specific anecdotal evidence, both contemporary (Waters, 2016; Starr, 2013) and historical (Russell, 1760), which suggests that cold water adaptation should be investigated as a non-pharmaceutical treatment for a range of conditions associated with chronic inflammation.

d. Immune function

Cold water swimmers claim to suffer fewer and milder infections as a result of the practice (Brenke, 1990). A boost to immunity from cold water is biologically plausible: CWI causes the release of stress hormones (Johnson *et al*. 1977; Kauppinen *et al*. 1989), and Dhabhar (2014) argues that short-term

stress readies the immune system to deal with injury or infection. Research into the effects of CWI on immune function has produced mixed results, possibly because participants and protocols varied from unacclimatised individuals taking a brief dip in ice-cold water (Dugué & Leppänen, 2000), to longer static CWI (Janský *et al*. 1996), to experienced long-distance swimmers training for eight hours (Kormanovski *et al*. 2010). In addition, different leucocytes and immunoglobulins (Igs) have been measured. Further, changes in immune system markers may not translate into altered *in vivo* defence (Castellani *et al*. 2002), and very few studies asked participants to report actual illness. A general weakness of research in this area is that many studies have small numbers of participants, and differences between male and female participants are often not reported. However, participant recruitment is difficult as cold water swimming is a minority activity and non-swimmers are often reluctant to undergo CWI.

If CWI does benefit immune function, then there should be improvements in both immune system markers and actual health over the course of an acclimatisation programme, and habitual cold water swimmers could have the most robust systems. However, there may be differences in the responses to static CWI and cold water swimming, as exercise and cold both cause physiological stress and their combined effect may exceed the individual effect of each (LaVoy *et al*. 2011).

The responses of the immune system to static CWI were investigated by Janský *et al*. (1996). Participants underwent an initial single immersion, followed by repeated CWI three times a week for six weeks, and the results are summarised in Table 1. It can be seen that adaptation altered both resting leucocyte numbers and their response to static CWI, both innate and adaptive cells being affected. However these changes were small and of uncertain significance, and repeated CWI did not alter the Ig response (Janský *et al*. 1996).

Brazaitis *et al*. (2014) immersed men intermittently as shown in Table 1, and found that there were differences between fast coolers (FC) and slow coolers (SC), with only the latter showing leucocytosis. Responses to static CWI appear to be strongly influenced by protocol and participants. The difference in leucocytosis between FC and SC may have resulted from SC having been immersed for a total of 120 minutes as against a mean of 96 minutes for FC, or from the two groups' differing responses to CWI. The use of alternating CWI and rewarming may also have complicated the physiological response. It seems also that the extent of the leucocytosis may correspond to the magnitude of the stress: Janský *et al*. (1996) found no increase in neutrophils after 60 min in water at 14 °C, while Brazaitis *et al*. (2014) reported a rise of 55% after a total of 120 min in 14 °C water with periodic rewarming.

The clinical significance of these findings is uncertain. Short-term leucocytosis arises from leucocytes leaving organs such as the spleen in response to the rise in catecholamines and cortisol, to be ready to deal with a threat (Dhabhar, 2014). Leucocytes are transferred in the blood to sites of potential infection, so arguably the most important part of this short-term response is a subsequent fall in blood leucocytes as they move into tissues such as the skin (Dhabhar, 2014). This has not been investigated in the context of CWI, however Yeager *et al*. (2016) found that monocytes and neutrophils did indeed migrate into sterile blister fluid in response to a dose of cortisol corresponding to that released during acute stress. The 29% rise in resting monocyte levels over six weeks of CWI reported by Janský *et al*. (1996) could indicate greater numbers in the body and a boosted immune system, but could also result from persisting presence in the blood rather than in sites of infection. Neither Janský *et al*. (1996) nor Brazaitis *et al*. (2014) considered actual illness, and both had only male participants.

Almost all the studies investigating the immune response to *dynamic* CWI have had participants who were experienced cold water swimmers, however there were wide variations in the swimming undertaken and the markers considered, and it is not possible to separate out the effects of exercise. Three studies asked swimmers to report colds or flu (upper respiratory tract infections, or URTI). URTI is a useful measure of *in vivo* immune function, being a very common infection which challenges both innate and adaptive elements (Hannigan *et al*. 2009).The results of all these studies are summarised in Table 1.

Dugué & Leppänen (2000) found that habitual cold water swimmers had higher resting levels of some leucocytes than non-cold habituated people. They also investigated the responses of both groups to brief dips in ice-cold water but, as this was after a sauna, it is not possible to separate the effects of the two thermal stresses. This was the only study to consider men and women separately, and there were differences between the sexes. However the small participant numbers make it difficult to establish the significance of these results.

Kormanovski *et al*. (2010) monitored 15 experienced long-distance swimmers for six months. Seven of the group completed three continuous long distance swims (LDS), one of 6 h (in month one) and two of 8 h (in months three and six), while the other swimmers rested (controls). All followed the same nutrition protocol. There were differences between the LDS group and the controls in leucocyte and Ig responses, over both the total study period and the LDS periods. The heavy training load may have slightly depressed base levels of leucocytes in the LDS group, but a training bout caused appreciable rises: granulocyte numbers rose almost fourfold during the 8 h.

The LDS group had significant decreases in resting levels of serum Igs and salivary IgA (sIgA) over the training period, while control swimmers did not. During all three LDS periods sIgA decreased markedly but remained unchanged in controls, while serum Igs showed no clear pattern in either group. As the authors point out, Ig levels are subject to considerable diurnal variation and can be considerably higher in the morning.

The sIgA result accords with decreases seen in dry-land athletes with a heavy training load (Mortatti *et al*. 2012), so may have been due to exercise rather than the cold. The usefulness of Igs as markers of *in vivo* immune function is not established: some studies have found a correlation between sIgA and URTI incidence (Gleeson *et al*. 2012), but others have not (Tiollier *et al*. 2005). None of the swimmers in this study reported an URTI during the six months' training or the three months afterwards, thus no relationship was found between immune markers and actual illness.

Lombardi *et al*. (2011) investigated unacclimatised participants completing a 150 m race in cold water, and found a significant increase in total leucocytes compared to the previous day. There was no control group, and while it is not possible to simulate CWI it would have been useful to take blood samples from non-immersed controls, as the stress of having blood taken could, in itself, affect immune markers (Dhabhar, 2014).

In the last two of these studies (Lombardi *et al*. 2011; Dhabhar, 2014) there seems again to be a link between the magnitude of the stress and the leucocyte response. The long-distance swimmers in Kormanovski *et al*. (2010) had no significant change in agranulocytes (most of which are neutrophils) after 1 h, but after 2 h numbers had increased by about 50 %, with a four-fold increase after 8 h. The unacclimatised swimmers in the study of Lombardi *et al*. (2011) showed the fastest response, with neutrophil numbers up 38 % after a 150 m race. However this was compared with the previous day, so some of the rise may have been due to race-day stress. All three studies report higher leucocyte numbers in cold water swimmers, but again it is not known whether these reflect greater numbers in the body or redistribution between different sites. The swimmers in the study of Kormanovski *et al*. (2010) were highly trained, and those of Lombardi *et al*. (2011) were unacclimatised and racing.

Other studies have focussed on recreational habitual cold water swimmers. Huang *et al*. (2011) compared middle-aged cold water swimmers with a sedentary group, and found that mononuclear cells from swimmers inhibited growth of leukaemia cells four times more effectively than those from controls. However the control group comprised sedentary adults rather than men undertaking a similar amount of dry-land activity, so did not control for effects of exercise, and the swimmers were much fitter than the controls ($\dot{V}O_{2max}$ 46.9 $mL.kg^{-1}.min^{-1}$ vs. 28.3 $mL.kg^{-1}.min^{-1}$). Teległów *et al*.

(2014) investigated 10 male winter swimmers and found no significant changes over the winter in their post-swim serum IgA, IgG or IgM. As blood samples were only taken after swimming, it is not possible to establish whether their response to immersion changed. There was also no control group of non-swimmers, making it impossible to distinguish between the effects of cold water and those of exercise.

Of all the above studies, only that of Kormanovski *et al*. (2010) reported actual illness in those exposed to cold water. In spite of alterations in immune markers, none of the swimmers suffered an URTI. However this was a small group of highly-trained individuals and so may not be representative of recreational cold water swimmers.

Two further studies investigated URTI incidence in habitual cold water swimmers. Brenke (1990) surveyed 85 regular ice swimmers, of whom 40 % stated that they suffered fewer, less severe and shorter infections than previously. In addition he followed eight patients at a remote rural practice and found a significant fall in consultations for flu-like illnesses. Collier *et al*. (2015) compared URTI incidence and severity in cold water swimmers with that in their cohabiting, but non-swimming, partners and with pool swimmers, and found that cold swimmers had fewer colds than their partners, but there were no differences between cold and pool swimmers.

All three studies that investigated URTI relied on participant self-report of illness. This has two possible drawbacks: first, it is difficult to remember having had colds in the past as Brenke (1990) asked participants to do; and secondly, many cold-water swimmers are deeply convinced that the practice is beneficial and so may under-report infections, whether consciously or otherwise. The swimmers in the study of Kormanovski *et al*. (2010) were monitored by a medic during their six months of training, but were asked to report URTIs in the three months that followed. Collier *et al*. (2015) reduced the likelihood of recall error by asking participants to report URTIs each week, but the possibility of biased responses remains.

In spite of the repeated claims for the benefits of cold water swimming, it is also possible that it may be detrimental in large doses. Collier *et al*. (2015) noted trends for positive correlations between cold water exposure and URTI incidence and severity, as shown in Table 1. If short-term stress is like an exercise that enhances the immune system's effectiveness, then prolonged stress could lead to fatigue and a reduced response. Dhabhar (2014) defines short-term stress as lasting minutes to hours, and chronic stress as being repeated for hours each day for weeks or months. Frequent cold-water swimming with prolonged shivering afterwards may fall into the latter category. Loria *et al*. (2014) found that regular winter swimmers had abnormal daily cortisol variations, and Dhabhar

(2014) comments that prolonged stress can lead to dysregulation of the diurnal cortisol cycle and to a suppressed immune response. Eccles & Wilkinson (2015) argue that both breathing cold air and chilling the body surface increase the likelihood of URTI, partly due to vasoconstriction in the nose. Exercise intensity may also be relevant; Wang & Huang (2005) found that exercise at 80 % $\dot{V}O_{2max}$ led to lymphocyte apoptosis. Oxygen consumption is greater in cold water and $\dot{V}O_{2max}$ is decreased (Tipton & Bradford, 2014), thus relative exercise intensity is increased. Physiological stress could also be affected by swim duration, air and water temperatures, body composition and extent of acclimatisation. These factors could act together to push the impact of cold water swimming on immune function from "benefit" to "detriment".

It is concluded that there is some evidence that the short stress of CWI may prime the immune system to deal with a threat, and thus be beneficial. Whether this effect is augmented by swimming has not been established, and may depend on the frequency, intensity, and duration of the exercise, among other factors. The disturbed diurnal cortisol rhythm seen by Loria *et al*. (2014) suggests that an excess of cold exposure may lead to continued physiological stress, and this could lead to immunosuppression. Thus, "optimum dose" of cold has yet to be determined, and is likely to differ between individuals. The definitive studies in this complex area await completion.

Table 1 Static cold water immersion (CWI) studies

Study	Participants	Protocol	Results	Actual illness?
Janský *et al*. (1996)	10 unacclimatised men	Initial immersion: 60 min at 14 °C Blood samples before and after CWI	Total leucocyte numbers: increased Individual types of leucocyte: no change Serum IgG: increased Serum IgA and IgM: no change	No
		Repeated immersions: As above, 3 x per week for 6 weeks Blood samples before and after each CWI	Total leucocyte numbers: unchanged from single CWI Pre- and post-immersion monocytes: increased CD25 T lymphocyte numbers: increased Pre- and post-immersion T and B lymphocytes: trend for increase Serum IgA, IgG and IgM: unchanged from single CWI	
Brazaitis *et al*. (2014)	40 unacclimatised men, divided into	Intermittent CWI (20 min at 14 °C	FC (n = 20): No changes	No

	fast coolers (FC, rectal temp reached 35.5 °C) and slow coolers (SC, reached 120 min total CWI)	followed by 10 min sitting in lab) until sooner of rectal temp 35.5 °C or 120 min total CWI Blood samples before and after CWI	SC (n = 20): Total leucocytes: increased % neutrophils: increased % lymphocytes and monocytes: decreased	

Table 2 Cold water swimming studies

Study	Participants	Protocol	Results	Actual illness?
Brenke (1990)	85 ice swimmers	Swam regularly for ≤ 5 min, water temp -1 – 4 °C Retrospective questionnaire	40% reported suffering fewer, less severe and shorter infections than previously	Yes
	8 patients at a remote rural practice, who began ice swimming	Swam for 5 – 6 year period Reported consultations for flu-like illnesses	Consultations fell from 0.88 per year before starting ice swimming to 0.5 per year at end of study period	
Dugué & Leppänen (2000)	Habitual cold water swimmers (5 women, 7 men) Controls, unacclimatised (6 women, 2 men)	Resting blood samples	Swimmers v controls: Female swimmers: higher leucocyte and neutrophil numbers Male swimmers: no difference in the above All swimmers: 50% higher monocyte numbers	No
Kormanovski *et al*. (2010)	15 experienced long-distance swimmers (8 men, 7 women), divided into long distance swim (LDS) group (4 men, 3 women) and controls (4 men, 4 women).	Carried out 6 months training, ≤ 160 km per month. LDS group completed continuous swims of 6 h (month 1) and 8 h (months 3 and 6), water temp 18 – 21 °C, while controls rested. All followed same nutritional protocol. Blood and saliva	LDS group v controls over 6 months: LDS group: trends for decreased resting granulocytes and agranulocytes (p = 0.099 and 0.059 respectively); decreased resting serum IgG and IgM and salivary IgA (sIgA) Controls: no changes LDS group v controls during the three LDS periods:	Yes

		samples before, during and after LDS period. Blood analysis and medical examination every 2 – 3 weeks during study period.	LDS group: granulocyte numbers increased; agranulocyte numbers rose then fell slightly; sIgA decreased; serum Igs: no change during first LDS, but fluctuated during second and third LDS Controls: no change in sIgA; increased serum IgA, decreased serum IgM in last 2 h of 8 h rest No swimmer had an URTI in the 6 month study period or the 3 months immediately afterwards	
Lombardi *et al*. (2011)	Unacclimatised individuals (13 men, 2 women)	150 m race in water at 6 °C Blood samples day before and straight after race	After race v day before: Total leucocytes: increased (especially neutrophils, monocytes and lymphocytes)	No
Huang *et al*. (2011)	Swimmers: 14 middle-aged men Controls: 11 sedentary middle-aged men	Swimmers swam 5 x per week (mean 55 min at moderate intensity), water temp 13 – 19 °C Resting blood samples	Swimmers v controls: Swimmers' mononuclear cells inhibited growth of leukaemia cells 4 x more effectively than those of controls	No
Teległów *et al*. (2014)	10 male winter swimmers	Swam regularly for 5 min, water temp ≤ 7.5 °C from Nov to Mar Post swim blood samples	Serum IgA, IgG and IgM: no change over study period	No
Collier *et al*. (2015)	21 habitual cold water swimmers and their cohabiting non-swimming partners 23 habitual pool swimmers and their cohabiting non-swimming partners	Weekly report of common cold symptoms for 13 weeks from December to March	Cold swimmers had fewer colds than their partners No differences between cold swimmers and pool swimmers	Yes

SUMMARY & CONCLUSION

The areas reviewed are presented in Figure 6. We have assessed the evidence-base for the claims made for CWI in each area using a modified version of the SIGN criteria (Scottish Intercollegiate Guidelines Network [SIGN], 2011).

INSERT FIGURE 6 ABOUT HERE

Other areas continue to evolve and are worthy of further study, included amongst these is the potential metabolic and thermogenic benefits associated with cold exposure and the activation of brown adipose tissue (BAT) (Blondin *et al.* 2014). The role that CWI and acclimation to CWI may have in this area remains to be investigated in humans, the closest investigators have come thus far is use of a water-perfused cooling suit to demonstrate that BAT acts as a non-shivering thermogenesis effector (Ouellet *et al.* 2012).

It is concluded that CWI is a significant cause of death internationally, and the physiological precursors to these deaths have been identified and investigated, although not fully described in all cases. The beneficial effects of CWI in terms of surviving prolonged immersion, cooling hyperthermic casualties, pre-CWI for enhanced performance in the heat, post-exercise CWI for recovery, and CWI adaptation as a treatment for inflammation-related condition or to boost the immune system all remain to be fully elucidated. Each of these areas have feasible rationales and hypotheses, but the areas are complex and the impact of CWI can vary from beneficial to detrimental depending on the subtle interplay of factors such as the: duration and intensity of cold water exposure; duration of post-CWI event; degree of hyperthermia; control condition adopted; potential benefit of inflammation; nature of the exercise to be performed. In short, for CWI, the evidence base for “kill” is currently somewhat more developed than that for “cure”.

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Figure Legends

Figure 1. Bathing machine, Germany 1893

Figure 2. A contemporary view of the initial responses to immersion and submersion in cold water ("Cold Shock"). Based on: Tipton 1989; Datta & Tipton, 2006; Tipton *et al.* 2010; Shattock & Tipton 2012. * Predisposing Factors include: Channelopathies; Atherosclerosis; LQTS; Myocardial hypertrophy; Ischaemic heart disease (reproduced from Tipton, 2016a).

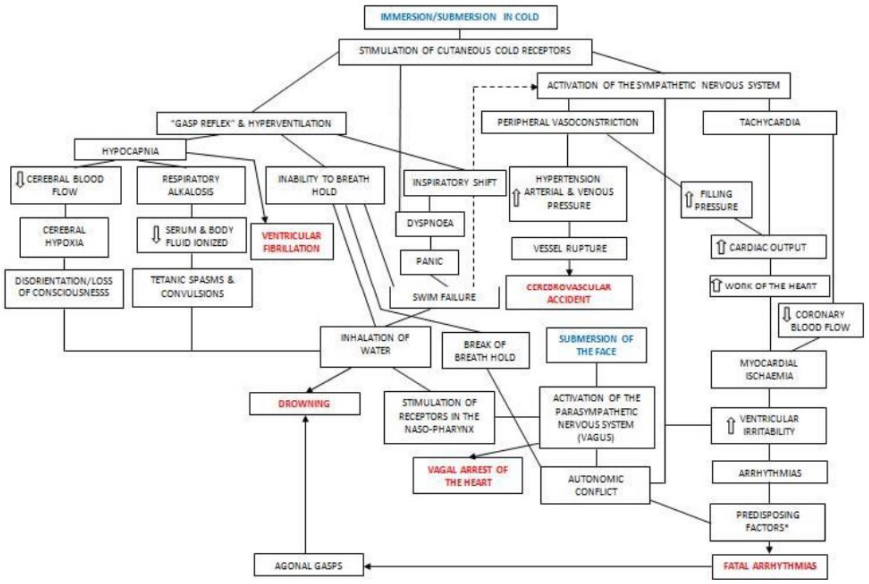

Figure 3. The "Physiological Pathways to Drowning" following immersion / submersion in cold water, with possible interventions for partial mitigation (dashed).
IS = Immersion suit; L J = lifejacket; EBA = emergency breathing aid (reproduced from Tipton, 2016b).

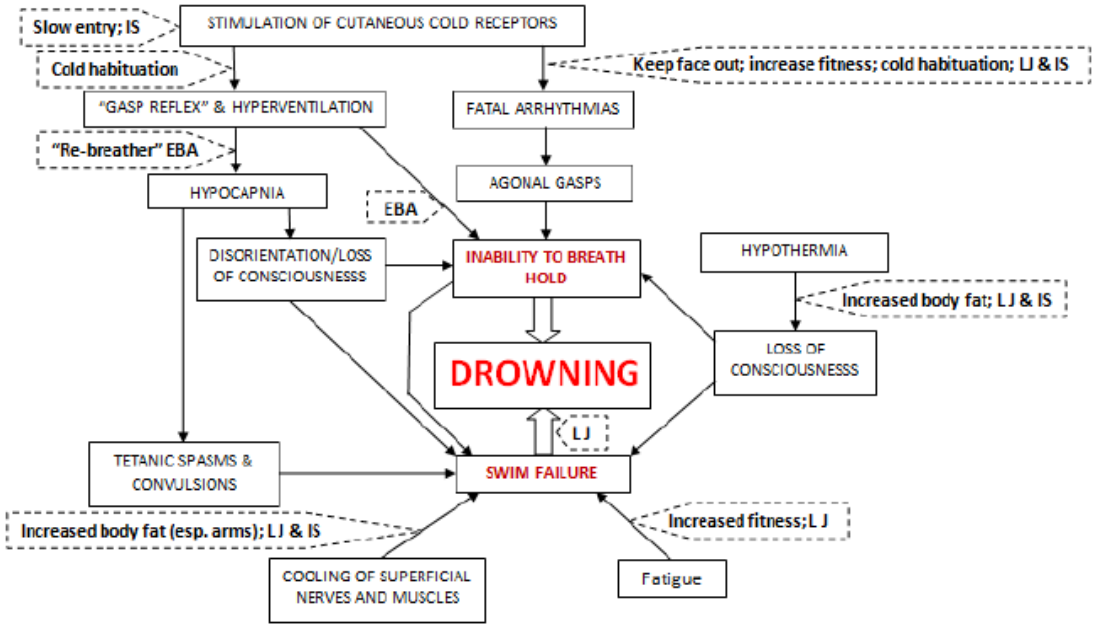

Figure 4. The possible positive and negative effects of post-exercise responses to cold water immersion.

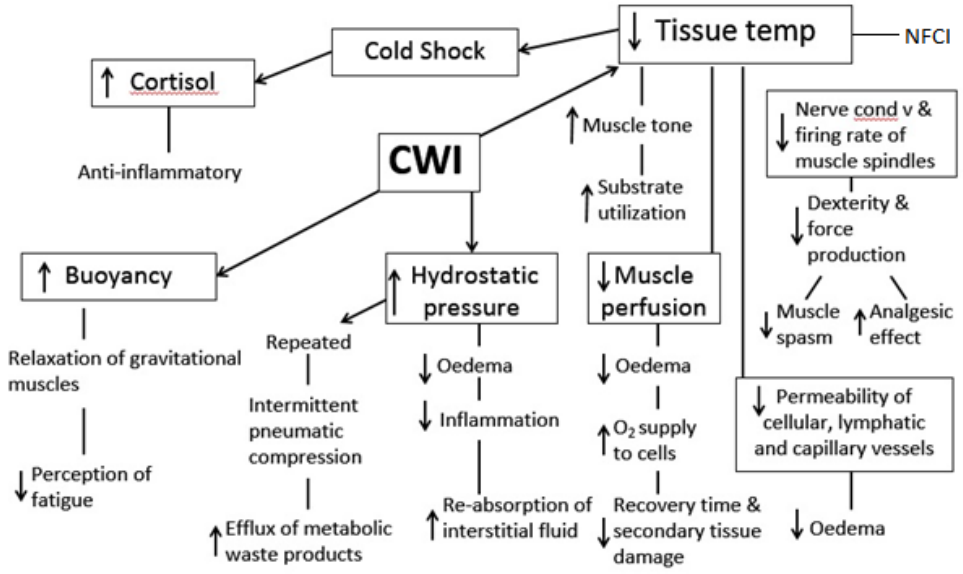

Figure 5. The hypothesised association between cold water immersion, inflammation and depressive disorders.

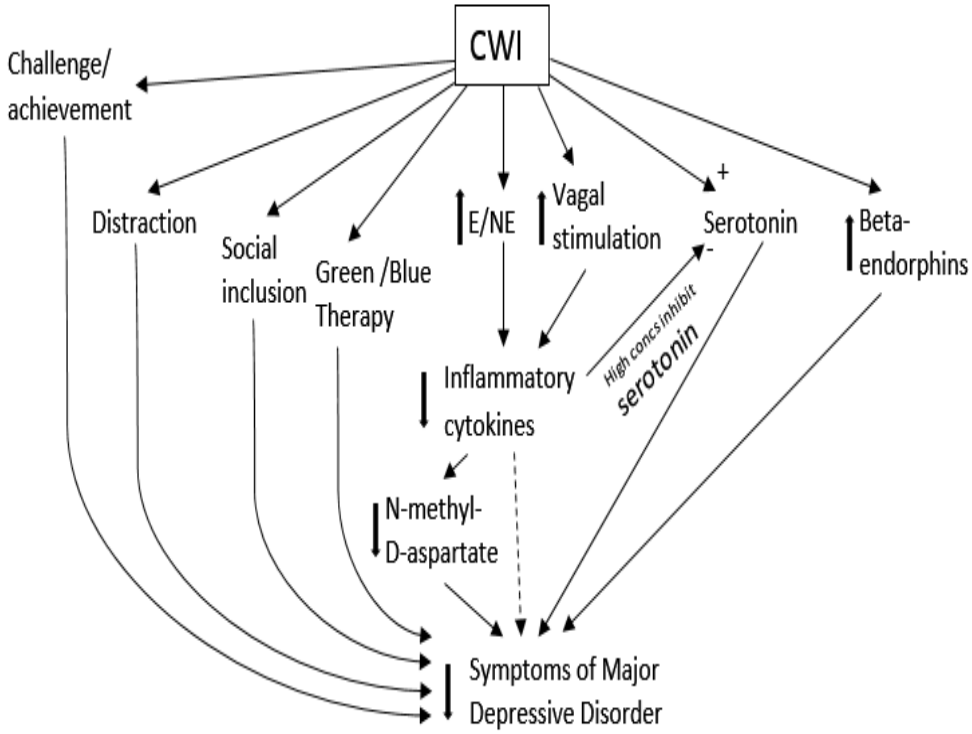

Figure 6. Cold water immersion: kill or cure. The responses in each category with a level of evidence assessment.