Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

Cold-water immersion

Evidence Summary

CWI may improve post-exercise muscle soreness, and studies have looked at potential effects on mood and inflammation. However, the data is limited. CWI has serious risks, especially if unacclimatized.

Neuroprotective Benefit: There is no clinical evidence to suggest that CWI can improve cognition or prevent neurodegenerative disease or decline. Studies have reported cognitive impairment from CWI, though many of these were long immersions.

Aging and related health concerns: CWI appears to improve delayed onset muscle soreness after exercise based on multiple systematic reviews and meta-analyses. Preliminary data suggest a benefit for mood, but more rigorous work is needed.

Safety: Adverse events like arrhythmias and decreases in cerebral blood flow have been reported with CWI, along with rare but serious events including death. Acclimatizing to CWI may help reduce risk. Cardiac conditions may be contraindicated with CWI.

Availability: Widely available at home, in physical therapy and fitness centers, and in other places with pools of water	**Dose**: The temperature range for 'cold water' varies, and the ideal temperature of the water, time of immersion, and part(s) of the body to submerge are not agreed upon. This is in part because these factors are interconnected; a shorter immersion in colder water may achieve the same degree of body cooling as a longer immersion in warmer water. Many studies focus on water temperatures of 10 to 15˚C; immersions should be under 30 minutes to mitigate risks of hypothermia.
Half-life: Not applicable	**BBB**: Not applicable.
Clinical trials: The largest meta-analysis identified included approximately 1,000 individuals.	**Observational studies**: Several small studies of 10 to 50 cold-water swimmers were identified.

What is it?

The practice of using cold temperatures for therapeutic purposes has a long history, with historical references going as far back as 3500 BC (Allan et al., 2022). Cold-water immersion (CWI), a form of cryotherapy, is the practice of submerging part or all of your body in cold water. What temperature is considered 'cold' varies, but CWI often involves water that is 15˚C (59˚F) or below. CWI can take place in a home bathtub, a specially designed cold plunge tub, a swimming pool, or other bodies of water such as rivers, lakes, and oceans. There are activities that are closely related to CWI, such as cold-water swimming, winter swimming, and ice swimming, the latter of which involves swimming in water between -2˚C and 9˚C, and contrast water therapy, which involves alternating between warm and cold water. Where possible, this report will delineate between these modalities.

As reviewed by Tipton et al., 2017, Farstad & Dunn, 2019, and Espeland et al., 2022, among many others, CWI can result in a range of physiological responses. The cold shock response is activated in sudden immersions of cold water, and can involve tachycardia, peripheral vasoconstriction, gasping for breath, and hyperventilating – the latter two of which can lead to drowning, particularly when the cold-water immersion is accidental or when the airway is under water. The strength of the cold shock

response correlates to the degree of skin cooling to a certain extent; it can occur with temperatures as high as 25˚C, peaks between 10 and 15˚C, and does not increase more at 5˚C. The diving response can also be activated if the face is submerged below the water as well. The diving response includes bradycardia, vascular splenic contraction, and adrenal release of catecholamines such as norepinephrine, epinephrine, and dopamine. Both of these reflexes involve autonomic nervous system activation, and there is a hypothesis in the field that coincidental activation of both reflexes may cause 'autonomic conflict' with both sympathetic and parasympathetic activation, which might lead to cardiac arrhythmias. Other responses include shivering and non-shivering thermogenesis.

Some of these physiological responses can be modulated through repeated CWI exposure, as acclimatization is known to occur. Cognitive preparation and physical adaptation can mitigate the respiratory aspect of the cold shock response, and physiological adaptions can lead to reduced catecholamine release, sensation of the cold, and resting body temperature, increases in parasympathetic activity, and delays in metabolic responses to cold and shivering. These effects have been observed after 4 one-hour sessions at 14˚C, and persisted for at least 2 weeks after termination of the cold adaption protocol (Janský et al., 1996; Farstad & Dunn, 2019).

There can be significant variation in response to CWI, both due to differences in CWI protocol such as duration, water temperature, body movement, time of day, and how much of the body is immersed, and differences in the individual receiving the treatment such as body fat composition, sex, race, age, fitness level, and level of acclimation. There can be a large variation in response even in a relatively homogenous group of individuals (Tipton et al., 2017; Norheim et al., 2018; Espeland et al., 2022).

Advocates for CWI suggest that the technique has a variety of health benefits, including improved immune system and metabolic function, decreased inflammation and pain, increased physical performance and recovery from injuries, and improved mood. It should be noted that these benefits can be challenging to prove experimentally. It is difficult, if not impossible, to blind individuals to this treatment, and studies indicate that perception can be a significant contributor to some outcomes. Observational studies are hampered by confounding factors, such as the possibility that healthier, happier people are more likely to engage in this kind of activity. Results of cold-water immersion may have other confounders; for instance, studies that look at outdoor cold-water swimming may reflect effects of exercise, being outdoors, or socializing rather than the cold exposure itself.

Neuroprotective Benefit: There is no clinical evidence to suggest that CWI can improve cognition or prevent neurodegenerative disease or decline. Studies have reported cognitive impairment from CWI, though many of these were long immersions.

Types of evidence:

- 2 meta-analyses or systematic reviews
- 14 clinical trials
- 1 review
- 1 laboratory study

Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function:

The effects of CWI on cognition are not clear. A systematic review of cold exposure and cognition identified 10 studies that looked at cognitive performance during or after immersion. The studies included 186 total participants, all of whom were healthy young adults with a median age under 30. The studies varied in terms of temperatures (4˚C to 15˚C), duration of exposure from (60 minutes to 180 minutes), and amount of body submerged (from legs only to the whole body except the head), as well as the type of cognitive testing performed, covering domains such as attention, executive function, memory, processing speed, visuospatial ability, and reasoning. Some studies did intermittent CWI with periods of rest at room temperature air in between CWI session whereas others involved a continuous immersion, and some studies did just one session while others did repeated sessions. Of these 10 studies, 9 found cognitive impairment, whether testing was done during or after immersion; some reported cognitive impairment even after core body temperature had returned to normal. However, these are very long exposures to cold temperatures, some purposefully designed to bring individuals to the brink of hypothermia. Whether these data reflect the effects of shorter immersions is not clear. Some of the included studies tested cognitive performance less than 30 minutes into the immersion; neither found improvements in cognitive performance (Falla et al., 2021). A small crossover study of 10 healthy adult men assessed cognitive performance during a 5-minute immersion up to the collarbone in 18˚C water or while sitting at room temperature. The participants performed significantly less well on the cognitive testing in the first 2 minutes of submersion compared to baseline and to their control performance in room temperature air (Stella & Morrison, 2022).

It is possible that the extent of immersion or type of cognitive function assessed might affect results. One small study of 28 healthy young men examined the effects of an acute stress on learning by using a 1 minute hand immersion in ice cold water, and found that participants subjected to the cold stress had improved learning performance on a classical conditioning paradigm and an assessment of spatial memory and reasoning as compared to control group participants (Duncko et al., 2007). Another small study of 33 healthy adults examined the effects of 5-minute immersion at 20˚C and assessed the impact on positive and negative affect as well as brain connectivity as measured by fMRI. The researchers found that participants felt more active, alert, and proud after the immersion as compared to baseline, and that there was an increase in brain connectivity between certain brain networks (Yankouskaya et al., 2023).

No studies appear to have assessed the effects of routine CWI on cognitive function. No studies have looked at the relationship between CWI and dementia diagnosis or cognitive decline.

Human research to suggest benefits to patients with dementia:

There are no studies assessing the effects of CWI in patients with dementia.

Mechanisms of action for neuroprotection identified from laboratory and clinical research:

It is not clear whether CWI would have neuroprotective effects; in fact, some studies report decreases in cognitive function during or after CWI, especially long CWI. However, there are several possible indirect and direct mechanisms by which CWI could affect brain health, including potential anti-inflammatory activities, improving mood, affecting brain connectivity, modulating overall stress response, and through actions of cold shock proteins.

Theoretically, if CWI could mitigate inflammation – particularly chronic inflammation – it could be neuroprotective. However, it is not clear if and how CWI is anti-inflammatory, as studies have found conflicting results. As reviewed in Tipton et al., 2017 and Espeland et al., 2022, among others, there are some data that suggest that CWI can modulate the innate immune system, with some studies finding increases in proportion of innate immune system cells after repeated CWI compared to baseline or individuals who do not engage in CWI, though some randomized trials have reported no changes after 3 weeks of CWI compared to the control group (Versteeg et al., 2023). Several studies have not found any change in cytokine levels or reported mixed results after repeated CWI. Some studies have reported

potential improvements in immune system function such as a study (n=3018) reporting reduced number of sick days in a group taking hot-to-cold showers as opposed to those taking hot showers, but it should be noted that this study was self-report data only, and there wasn't a significant difference in number of days someone felt ill (Buijze et al., 2016). These effects may also depend on the extent of cold shock, age of individual, or other factors, with one study finding more inflammatory markers and autophagic dysfunction under cold stress conditions in older men compared to younger men (King et al., 2024).

Depression is a known risk factor for dementia. Mood improvements are one of the more commonly reported anecdotal benefits of CWI, though significant research work is needed in this area. It is not clear how the improvements in mood are mediated; it may be due to aspects of the initial stress response such as increases in catecholamines or changes in cortisol, or increases in β-endorphins, changes in brain connectivity, or another, yet to be discovered mechanism (Reed et al., 2023; Yankouskaya et al., 2023).

There is preclinical speculation that cold shock proteins may play a protective role. Cold shock proteins, as the name implies, respond to cold shock to maintain homeostasis. Some of these proteins are also active during hibernation. Many are RNA/DNA-binding proteins that facilitate the transcription and/or translation of target mRNAs. One cold shock protein, RBM3, is thought to be involved in a number of important cell processes such as regulating apoptosis, metabolism, and response to oxidative stress. Preclinical studies using cold-stress in an AD model have suggested that RBM3 might be directly neuroprotective, including through prevention of synaptic and neuronal loss in stress situations and in enhancing synaptic plasticity, including in neurodegenerative disease models. These are very preliminary findings, and RBM3 has also been implicated in cancer progression, so will require significant further study (Peretti et al., 2015; Hu et al., 2022).

There are also theories that acclimatizing to the stressor of cold can help acclimatize to other stressors. However, more research is needed to explore these theories and disentangle the many complex contributing factors to response to cold, including age, sex, temperature, and duration of CWI, and identify biologically meaningful effects.

APOE4 interactions:

It is not known whether cold-water immersion has any interaction with APOE4 status.

Aging and related health concerns: CWI appears to improve delayed onset muscle soreness after exercise based on multiple systematic reviews and meta-analyses. Preliminary data suggest a benefit for mood, but more rigorous work is needed.

Types of evidence:

- 7 meta-analyses or systematic reviews
- 4 clinical trials

The effects of CWI on aging and health-related conditions are largely not known. Most work has focused on CWI in relation to exercise, though some small studies have also started to assess the impact of CWI on mood.

Recovery After Workout: PROBABLE BENEFIT FOR MUSCLE SORENESS, POSSIBLE HARM TO MUSCLE GAIN

Use of CWI as a performance enhancement for, or recovery modality after, exercise is perhaps the most studied effect of CWI. Multiple systematic reviews and/or meta-analyses, including a Cochrane systematic review, have found that CWI may reduce delayed onset muscle soreness (DOMS) after exercise when compared to passive interventions of rest or no intervention (Bleakley et al., 2012; Xiao et al., 2023; Batista et al., 2023). Batista et al., 2023 included 44 studies of CWI as defined by water between 5 and 15˚C or less, and the authors were able to assess the effects of water temperature and immersion times on DOMS; they found that compared to control, CWI was effective regardless of water temperature and protocol, and that short (10 minutes or less) and medium (11 to 15 minutes) immersions were effective compared to control but not immersions longer than 15 minutes.

Groups have also assessed whether CWI has other benefits for exercise, or benefits for only particular kinds of exercise. Some systematic reviews and meta-analyses have suggested that CWI may attenuate gain in muscle (Malta et al., 2021; Grgic, 2023). The data suggests that CWI may be most effective for endurance or aerobic exercise recovery, not strength training, though ultimately this depends on the goals of the exercising individual, including when they plan to exercise next.

One important note is that muscle soreness is subjective and that these studies cannot be blinded. The placebo effect may account for at least some of the perceived benefit of CWI (Nasser et al., 2023; Batista et al., 2024).

Depression and Mental Health: POTENTIAL BENEFIT FOR DEPRESSION

Anecdotally, many people report mental health or mood benefits from CWI. On one hand, there are many possible mechanisms through which CWI could improve mood, including catecholamine release during CWI, contributions of exercise or being outside during cold-water swimming, and a feeling of pride, satisfaction, or resilience from completing a physically difficult task. Staying in cold water might require mindfulness techniques or other cognitive re-framings that can improve mental health. On the other hand, it is difficult or impossible to separate out a potential placebo effect as it is not possible to blind people to this intervention. There are also few studies looking at CWI and mood, and many of them involve outdoor cold-water swimming, which has several confounding elements.

Studies have reported increased positive affect and/or reduced negative affect from single CWI sessions of 15 minutes or less (Reed et al., 2023; Yankouskaya et al., 2023). A 2020 study assessed the effects of a 10-week introductory outdoor swimming course on 61 swimmers compared to 22 controls; the control participants were friends and family members of the swimmers and sat on the beach during the swimming sessions. The authors report that both swimmers and control participants had improvements in mood and well-being scores as compared to baseline, but the improvements were significantly greater in swimmers than in the control group (Massey et al., 2020). Other studies have reported improvements in mood after just one cold-water exposure compared to their own baseline or to a control group (Kelly & Bird, 2021; Yankouskaya et al., 2023).

Like the findings for muscle soreness, these results are complicated by the fact that mood is subjective, and the intervention cannot be blinded. Moreover, the two studies discussed above with control groups were not randomized; the participants self-selected. Further work is needed to clarify the effects of CWI on mood.

Safety: Adverse events like arrhythmias and decreases in cerebral blood flow have been reported with CWI, along with rare but serious events including death. Acclimatizing to CWI may help reduce risk. Cardiac conditions may be contraindicated with CWI.

Types of evidence:

- 1 systematic review

- 3 clinical trials
- 6 reviews
- 2 Peter Attia podcast episodes
- 1 news article

Cold-water immersion has the potential to have serious consequences, though it can be challenging to quantify these. There have been deaths from CWI reported in news outlet (The Guardian; Sky News), though these appear to be rare events. Not all studies collect or report adverse event data, and some studies use much longer immersions or cold-water swimming immersions, both of which may not be fully relevant to a purposeful, short immersion of part of the body in a tub. Many CWI studies also involve healthy young adults, particularly athletes, which may or may not reflect effects in older individuals or non-athletes, especially as some studies find differences in cold response based on age or aerobic fitness level. Accidental CWI is dangerous, and even purposeful outdoor cold-water swimming can have additional hazards such as drowning. Cold-water swimming should never be done alone.

A study of 3018 individuals 18 to 65 years of age who were randomized to hot-to-cold showers or hot showers only did report adverse events. The study reported 20 serious adverse events, none of which were thought to be related to the hot-to-cold showers. The most common events thought to be related to the cold shower were persistent cold sensation in body (196 participants) or hands and/or feet (257 participants). Other adverse events reported in 10 or fewer participants included muscle aches or cramps, itching, insomnia (potentially related to cold shower in evening), dizziness, lower back pain, headache, nose bleeding, diarrhea, palpitations, and transient swelling and erythema in one hand (Buijze et al., 2016).

The body has known physiological responses to the cold, including tachycardia, peripheral vasoconstriction, and other adaptations to try to maintain temperature homeostasis (Tipton et al., 2017; Stella & Morrison, 2022). It is not clear whether these cardiac changes are clinically meaningful, though it may depend on the age and health condition of the participants. One study of 33 healthy adults assessed the impact of a 5-minute immersion in approximately 20˚C water and as expected, found significantly increased heartrate and respiratory activity during immersion compared to baseline. One immersion had to be stopped early due to 'many' ectopic beats detected on ECG (Yankouskaya et al., 2023). Another study examined cardiac responses in healthy young men by recording ECG traces during helicopter underwater escape training. This training involves brief immersion (~4 minute period in the water, 10 second 'escape' including face under water, and 40 second post-submersion period) in 29˚C

water. The 26 male volunteers completed a combined total of 130 runs, 126 ECG traces could be analyzed, and 32 cardiac arrhythmias were identified in 22 participants. All but 6 of these arrhythmias were during the submersion. Aerobic fitness was inversely correlated with occurrence of an arrhythmia. While these arrhythmias were asymptomatic and thought to be of little clinical significance, it is not clear whether this would be the case in older or less fit individuals, or those in colder water for longer (Tipton et al., 2010).

One small study of 13 men assessed cerebral blood flow during a 30 second immersion in 0˚C water. The authors report that cerebral blood flow was significantly decreased, and two of the thirteen participants experienced symptoms such as drowsiness, blurred vision, and loss of responsiveness that were thought to be related to the change in cerebral blood flow (Mantoni et al., 2007).

Though the literature has gaps in terms of quantifying safety information, the overall conclusion is that individuals should discuss CWI with their doctor before engaging in CWI, even if the CWI is in their bathtub. This is especially true for individuals with a history of cardiac conditions or who are on medications that affect the cardiovascular system. Deaths from CWI are thought to stem primarily from cold shock responses; as acclimatizing to cold water can mitigate some of the shock response, easing into CWI may be useful. Acclimatizing can include a slow and controlled entry into the water, splashing water on the body before full immersion, and starting at less cold temperatures and shorter durations (Kelly & Bird, 2021).

Drug interactions:

There are no known drug interactions with CWI. CWI may require additional monitoring or may not be appropriate for every individual based on their medical history; anyone considering CWI should speak with their medical professional(s) before trying the intervention. Cardiac conditions like long QT syndrome, ischemic heart disease, myocardial hypertrophy are thought to be contraindicated with CWI, given the risk of arrythmia. Blood pressure modulating medications may also add risks to CWI, as they may affect cold shock response (American Heart Association). Individuals with cold allergies or Reynaud's should also be cautious about CWI (Bleakley et al., 2012).

Research underway:

According to clinicaltrials.gov, there are 7 ongoing trials that are investigating the effects of cold-water immersion on some aspect of physiology or for a particular population. There are no ongoing clinical trials of cold-water immersion for cognitive function, dementia, or any related condition.

Search terms:

Pubmed, Google: cold-water immersion

- Dementia, safety, cognition, safety, mood, depression, adverse events, exercise

Websites visited for cold-water immersion:

- Clinicaltrials.gov
- Examine.com