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.

Whole Body Cryotherapy (WBC)

Evidence Summary

WBC may provide short-term perceived benefits for specific inflammatory or muscle recovery conditions, but the challenges in study design make it difficult to draw any firm conclusions.

Neuroprotective Benefit: Little evidence suggests it would be beneficial for neurodegenerative disorders, though it may provide short-term symptomatic relief for patients with MS or depression.

Aging and related health concerns: There is some evidence that WBC might provide short-term perceived benefit for certain inflammatory conditions and for exercise recovery, but it is not clear whether it has any benefit above other therapies.

Safety: Risks of PBC and WBC can include frostbite, headache, increased blood pressure, and cold panniculitis. Inappropriately administered cryotherapy can increase risks. Many studies do not report adverse events, making it difficult to fully assess safety.

Availability: Widely available for use in spas and gyms that specialize in whole-body cryotherapy	**Dose**: Multiple sessions of short (~1-5 minute) duration at -100˚C to -190˚C; temperature may vary based on type of chamber used.
Half-life: N/A	**BBB**: N/A
Clinical trials: Dozens of small studies examining groups of ~20 to ~100 participants were identified.	**Observational studies**: No observational studies of whole-body cryotherapy were identified.

What is it?

Using cold temperatures as a therapeutic modality has been around for millennia, and ranges from local application of ice packs to cold water immersion to whole-body cryotherapy (WBC). Whole-body cryotherapy was invented in 1978 by Toshima Yamauchi, a Japanese doctor who used it to treat rheumatoid arthritis. It involves exposure to dry cold, often between -100˚C to -190˚C, for a short period of time, usually 1 to 5 minutes, by stepping into a chamber. Sometimes the technique is called cryostimulation when used for athletic recovery and cryotherapy when used to treat a medical condition, though terminology is still evolving. This report will use the term cryotherapy as the technique is the same. Partial-body cryotherapy (PBC) is a variant of WBC; in PBC, the head is outside of a chamber, but the body is inside the chamber. In either version, individuals cover all extremities (hands, feet, ears, etc.) before entering the chamber (Bleakley et al., 2014). PBC typically involves a liquid-nitrogen cooled cryochamber that exposes participants to nitrogen gas and the concomitant confounding factors and risks thereof such as hypoxia, whereas WBC cryochambers are cooled via closed systems that do not expose the user to nitrogen gas. The two methods have potential differences in chamber temperature, with PBC often being colder, though there is also potential for heterogeneity of temperature within the chambers for both techniques. Some groups posit that PBC may have greater temperature variation within the chamber. While this report will discuss both techniques, it should be noted that some groups think the two techniques should be considered separately due to these differences (Legrand et al., 2023).

Cryotherapy is purported to reduce inflammation, decrease tissue temperature, have an analgesic effect, improve sleep, and enhance recovery after exercise. Both forms of cryotherapy have many

reported uses including rheumatoid arthritis, fibromyalgia, ankylosing spondylitis, multiple sclerosis, chronic lower back pain, depression and anxiety, inflammation, and muscle damage recovery (Bleakley et al., 2014). Websites promoting these kinds of cryotherapy will often make further claims.

Unfortunately, several issues weaken the evidence for WBC. First, there is no clear way to run a placebo-controlled trial. Some investigators attempt to use a comparator therapy, such as different temperatures (e.g. -30˚C vs. -120˚C) or different time durations (e.g. 1 minute vs. 5 minutes); whether these are truly placebos is difficult to say. Other studies use no treatment as a control or compare WBC to other forms of cold therapy, such as cold-water immersion, neither of which allow for blinding of participants. Perception bias could significantly impact results, particularly for self-report assessments. Others have conducted cross-over studies. Still other studies are open label. Not all studies report adverse events. Most studies include few participants, adding an additional complexity to data analysis. Neither WBC nor PBC is cleared or approved as safe or effective for any condition (FDA).

Interestingly, most of the studies concerning disease states (e.g. depression, dementia, rheumatoid arthritis, etc.) were conducted in Poland.

There are approved forms of cryotherapy, such as cryosurgery for different types of lesions, and therapeutic cooling can be standard care protocol for certain conditions like hypoxic-ischemic encephalopathy in newborns. These versions of cryotherapy are very different and not within the scope of this report.

Neuroprotective Benefit: Little evidence suggests it would be beneficial for neurodegenerative disorders, though it may provide short-term symptomatic relief for MS and depression subjects.

Types of evidence:

- 1 systematic review and meta-analysis
- 2 randomized controlled trials
- 2 non-randomized clinical trials
- 5 studies in multiple sclerosis
- 4 studies in depression

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

One open-label study investigated the effects of WBC in patients with mild cognitive impairment (MCI) (n=unknown). After 10 sessions, cognitive function improved ($p<0.05$), especially memory, plasma nitric oxide (NO) increased ($p<0.05$), BDNF increased ($p<0.05$), and IL-6 decreased ($p<0.05$). The paper is inaccessible and was published by a group in Poland (Rymaszewska et al., 2018).

In 2021, the same group published results from a randomized controlled trial of WBC in patients with MCI (Rymaszewska et al., 2021). In total, the trial randomized 86 WBC-naïve patients to either WBC or control group, both of which involved 10 sessions over the course of 2 weeks. The temperatures for the two conditions are detailed below:

Group	Acclimation Temp (30 seconds)	Main Session Temp (2 minutes)	Acclimation Temp (30 seconds)
Placebo	-20˚C	-50˚C	-20˚C
WBC	-60˚C	-110˚C the first session; -135˚C at following sessions	-60˚C

Of the 86 randomized patients, 62 completed the 10 sessions: 33 in the WBC group, and 29 in the control group. The study utilized three measures of cognition: DemTect, SLUMS, and Test Your Memory (TYM), all three of which are validated for Polish speaking populations. DemTect is thought to be particularly sensitive to memory deficits. SLUMS and TYM both test around 10 cognitive areas such as orientation, arithmetic skills, concentration, and abstract thinking. Patients were tested at baseline, after the 10th treatment session, and 2 weeks after the end of treatment. The investigators also assessed quality of life and psychiatric symptoms such as depression and collected blood samples to examine markers of inflammation.

There were some statistically significant cognitive differences at baseline on certain cognitive scales or subscales, such as a significantly better overall score in the experimental group as measured by SLUMS ($p=0.03$) and a difference on the semantic fluency subscale of the DemTect assessment ($p=0.04$; data on direction not accessible). When the researchers looked at the change in cognitive function, the experimental group had a statistically significant improvement from baseline to the end of the

approximately 2-week treatment period as compared to the control group (p=0.01). The effect did not persist to the third testing timepoint which occurred 2 weeks after the end of testing. Based on self-report data from patients, those in the WBC group appeared to have a reduction in depressive symptoms as compared to the control group. There was no significant change or difference in any plasma inflammatory marker (IL-6, IL-10, NO, CRP) between the groups over the course of the trial. There was, however, a significant decrease in plasma BDNF levels in the experimental group as compared to the control group ($p<0.05$).

A 2021 randomized controlled crossover study assessed the effects of partial-body cryotherapy in 18 healthy young adults on measures of cognition, cerebral oxygenation, and parasympathetic cardiac control. Half of the participants were men and half were women. The study consisted of three visits: 1 familiarization, 1 control condition session, and 1 partial body cryotherapy session, and the order of control vs. PBC sessions was determined by coin-flip for each participant. During the session, the patient would rest, then perform a Stroop test, then stand in the cryochamber at either room temperature (approximately 20 to 21˚C) or at -150˚C for 3 minutes, then perform a second Stroop task. The Stroop test is thought to reflect executive processing, selective attention capacity, and processing speed. Data on heart rate via monitor and cerebral oxygenation via Near-Infrared Spectroscopy were collected. The researchers reported that in the men only, the reaction time on the Stroop test was significantly decreased after PBC as compared to pre-PBC. Increases in heart rate variability were observed in men and women after PBC as compared to control, though to a greater extent in men. There also appeared to be increased cerebral extraction of oxygen in men only after PBC, as compared to the control session. One possible explanation for the blunted physiological response in women is autonomic responses to cold temperatures may be due to heat loss triggered vasoconstriction. As women tend to have a higher body fat percentage, their response to the same temperature and time of cold exposure may be different than men. The study has caveats, including the technical limitations of NIRS and the small sample size, and the intrinsic lack of blinding (Theurot et al., 2021).

Another 2021 study examined the effects of whole-body cryotherapy in 84 older adults who had subjective cognitive impairment who were either cognitively intact or had MCI based on scores on the MoCA cognitive assessment. This 9-week study had three groups: a standard care group, a group who received computerized cognitive training (CCT) and psychoeducation, and a group who received computerized cognitive training, psychoeducation, and 10 sessions of WBC. It is important to note that this study was not randomized; participants who were unable to attend regular sessions were assigned to the control group, and participants without contraindications were assigned to the CCT + WBC group.

The WBC sessions consisted of a 2-minute session at -110˚C on the first day and -130˚C on subsequent days, with 30 second acclimations at -60˚C before and after the 2-minute session. The authors report that multiple factor analysis showed significant change in general cognition over time in the intervention groups as compared to the control group ($p<0.05$) and improvements on several subdomains of cognition, but there was no difference between the experimental groups. The authors also report that there was a significant reduction in depressive symptoms in the CCT + WBC group over time, but not in the other groups. The improvement in depressive symptoms was not associated with cognitive improvement, and so the authors hypothesized that the effect on depressive symptoms was mediated by WBC. It should be noted that the group receiving WBC may have been healthier though, as they did not have contraindications to WBC (Senczyszyn et al., 2021).

Human research to suggest benefits to patients with dementia:

The effects of partial- or whole-body cryotherapy in patients with dementia are not known.

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

While the potential neuroprotective mechanism of action of WBC or PBC is not known, there are several common hypotheses in the field. The primary theories are that cryotherapy is neuroprotective by increasing antioxidant capacity or otherwise reducing oxidative stress, reducing inflammation, and affecting lipid metabolism (Misiak and Kiejna, 2012). Other theories include activating homeostatic mechanisms and modulating autonomic system function (Bleakley et al., 2014). It should be noted that many of these hypotheses rely on lowering the temperature of body tissue, and WBC is not necessarily superior to other cold therapy techniques at reducing body temperature. Ice pack application appears to be associated with greater drops in skin temperature than WCB or cold-water immersion, for instance. It is not clear whether WBC reduces temperature better than cold-water immersion (reviewed in Bleakley et al., 2014).

There are conflicting reports on the effect of WBC on some of these potential mechanisms. Several studies have examined levels of inflammatory markers such as IL-6, IL-10, IL-1β, and CRP, but have reported very different findings (Krueger et al., 2019; Śliwicka et al., 2020; Wiecek et al., 2021; Rymaszewska et al., 2021). It is difficult to assess whether this is due to small sample size, different patient populations, different cryotherapy protocols, or lack of biological efficacy.

APOE4 interactions:

None reported.

Other neurological disorders

Multiple Sclerosis (MS)
Sixty patients with MS were randomized to WBC, physical exercise (PE), or WBC followed by physical exercise (WBC+PE). WBC consisted of 10 sessions over 2 weeks. Physical exercise consisted of a 60-minute session using resistance bands. General well-being improved for the PE and WBC+PE groups, depression was reduced for the WBC and WBC+PE groups, anxiety was reduced for the WBC+PE group, and mobility improved for the WBC group (Pawik et al., 2019). A 2021 study of 114 patients with MS assessed the impact of WBC on various measures of function. Patients were randomized to no treatment or 20 sessions of WBC over the course of 4 weeks and change from baseline to end of treatment was assessed. No change was observed in the control group. Treatment with WBC was associated with gait improvement, decreased fatigue, and increase in grip strength over the course of the trial; they did not compare results between groups. The authors posit that this may be due to bioelectric changes in muscle (Radecka et al., 2021).

Similarly, an open-label study of 24 MS patients showed that 10 sessions of WBC improved functional status and feelings of fatigue (Miller et al., 2016). Ten sessions of WBC also improved functional status and reduced levels of uric acid in secondary progressive MS patients in an open-label study, an effect that lasted 3 months later (Miller et al., 2013), and increased total antioxidant status in secondary progressive MS patients (Miller et al., 2011).

Depression
A systematic review and meta-analysis published in 2021 assessed the effects of whole-body cryotherapy on mental health. The study included 10 studies of WBC in human adults that assessed mental health in some way. The 10 studies had a combined total of 294 participants. The authors found that WBC was associated with a decrease in depressive symptoms and an improvement in reported quality of life. However, there was considerable heterogeneity. Additionally, many of the included studies were not randomized or had other methodological issues that hampered comparison, such as using different WBC protocols (Doets et al., 2021).

Aging and related health concerns: There is some evidence that WBC might provide short-term perceived benefit for certain inflammatory conditions and for exercise recovery, but it is not clear whether it has any benefit above other therapies.

Types of evidence:

- 2 meta-analyses or systematic reviews
- 1 systematic review
- 1 scoping review
- 12 clinical trials
- 5 studies in rheumatoid arthritis
- 3 studies for pain
- 3 studies on heart rate variability
- 2 studies on sleep after elite athlete exercise

Recovery after workout or sports injury: POTENTIAL SHORT-TERM BENEFIT

Rose et al., 2017 conducted a systematic review of the effects of WBC after damaging exercise-induced muscle injury in healthy, physically active subjects (not a specific injury; rather, the normal muscle injury that occurs with heavy exercise). The review found 16 papers on the topic. All participants were exposed to WBC for 2-3 minutes with varying repeated exposures of 1-30 sessions over 1-10 days. The articles were separated into "Laboratory controlled studies" (a single exercise session) or "Applied studies" (those where WBC was part of routine training). A summary of the results is to the right.

Laboratory controlled studies (10)

The four studies that used multiple WBC exposures found a significant decrease in muscle pain and an increase in muscle function.

- *Muscle function:* Most of the studies that used one WBC treatment did not see an increase in muscle function.
- *Pain:* Of the studies that examined pain, only those where WBC was administered immediately after exercise showed a reduction in pain.
- *Muscle damage:* Muscle damage was measured by levels circulating creatine kinase. There was a dose-response relationship, where more WBC treatments were associated with less muscle damage.
- *Inflammation:* All studies showed a decrease in inflammation (measured by plasma cytokines) after WBC.

Applied studies (6)
All "Applied studies" used multiple WBC treatments, with an average of 15 exposures.

Studies of acute usage of single-session WBC have largely reported no benefits. Abaïdia et al., 2017, Russel et al., 2017, Wilson et al., 2018, Krueger et al., 2019, and Hohenauer et al., 2020 all report little to no benefit of WBC on blood measures of inflammation or assessments of muscle function compared to cold-water immersion or control group, depending on the trial. Some studies such as Wilson et al., 2018 report potential negative effects of WBC on muscle function. Benefits were typically limited to perception of reduced muscle soreness, and this reduction was not significantly improved as compared to cold-water immersion.

Rheumatoid Arthritis (RA): POTENTIAL SHORT-TERM BENEFIT, POSSIBLY NOT BETTER THAN STANDARD OF CARE
A 2022 study randomized 64 patients with RA who were also receiving a separate multimodal RA treatment to either no additional treatment or 6 sessions of WBC (3 minutes, -130˚C) over the course of 2 weeks; 56 participants completed the trial. Pain significantly improved in both groups from baseline, but the group receiving WBC had greater pain improvements; the change in the WBC group was significantly more than in the no additional treatment group. Pain levels were significantly lower than baseline in the WBC group at a 12 week follow up. Other measures of disease activity and function showed significant improvements in the WBC group at the end of treatment, though these were not significant at the 12 week follow up. The authors speculate that this could be due to significant decreases in serum levels of IL-6 and TNFα that they detected in the intervention group from baseline to the end of treatment, though there was not a statistically significant difference in levels of these cytokines between the control and intervention group (Klemm et al., 2022). Forty-four postmenopausal women with RA were randomized to WBC (3 min) or a traditional rehabilitation program with other physical agents (magnetotherapy, electrotherapy, ultrasound therapy, and laser therapy) for two weeks. Procedures were carried out each weekday along with a kinesitherapy program. All clinical measures (pain, fatigue, inflammation, etc.) were improved in each group though WBC was not better than traditional rehabilitation programs (Gizinska et al., 2015). In another study, 40 patients with RA were randomized to WBC (-110°C) or WBC (-60°C). After seven days (3 treatments per day with 2 on the last) there were decreases in disease score activity (DAS) and pain in both groups, with pain being significantly more reduced in the WBC -100°C group (Hirvonen et al., 2006; Bouzigon et al., 2016). Forty patients with RA also received either WBC (-160°C) or cold air flow (-30°C) over 10 days. Both groups showed improvements in clinical outcomes and a reduction in TNFα levels (though no change in IL-6),

with no difference between groups (Jastrzabek et al., 2013). Finally, 20 patients with RA underwent daily WBC or conventional therapy for four weeks. There were reductions of histamine in the WBC group with no reductions in measures of neutrophil activation or markers of cartilage metabolism in either group (Wojtecka-Lukasik et al., 2009).

Pain: POTENTIAL SHORT-TERM BENEFIT
In an open-label study in 50 patients with osteoarthritis, 10 daily WBC treatments reduced the intensity of pain, the incidence of pain, the limitation of physical activity, and reduced the number of patients on pain killers (Chrusciak, 2016). Ninety-six elderly male patients suffering from chronic lower back pain were randomized to physical activity or WBC + physical activity. Over 3 weeks, those who underwent WBC prior to physical activity had a greater range of lumbar spine motility (Giemza et al., 2014). Another study from the same group compared WBC twice a week to WBC daily for 3 weeks in elderly men with lower back pain and found that only daily treatment improved lumbar spine mobility (Giemza et al., 2015).

Autonomic nervous system: POTENTIAL SHORT-TERM BENEFIT
Eleven elite synchronized swimmers performed two water ballets separated by 70 minutes with either WBC, contrast-water therapy (CWT), active recovery (ACT), or passive recovery (PAS). After the first ballet, heart rate variability (HRV) was decreased and went back to baseline after CWT, ACT, and PAS. WBC increased HRV 2- to 4-fold (Schaal et al., 2012). Forty healthy men underwent either WBC, PBC or no treatment. HRV increased after PBC (effect size = 0.60) and WBC (ES = 0.52) (Hausswirth et al., 2013). Similar results were found in a follow-up study from the same group with PBC increasing the Root Mean Square of the Successive Differences (RMSSD – a measure of HRV) by 49.1% and WBC increasing RMSSD by 38.8% (Louis et al., 2015).

Sleep: REVERSES NEGATIVE IMPACT OF EXTREME TRAINING
In a cross-over trial, 10 elite swimmers underwent two 2-week high intensity training sessions, one of which was followed by WBC. Sleep latency in the control session increased by 11 minutes, sleep duration decreased by 21 minutes, and sleep efficiency decreased by 1.9%. In the WBC session, there were no significant differences in sleep latency or sleep duration, though sleep efficiency decreased by 1.6% (Schaal et al., 2014). In another study in 27 elite basketball players, a single session of PBC increased perceived sleep quality by 15% (Bouzigon et al., 2016).

Obesity, Weight Loss, and Lipid Profiles: UNCLEAR BENEFIT

A 2022 scoping review assessed the potential effects of WBC in obesity. The authors included 8 articles in their review. Many of the included studies examined markers of inflammation, body composition, and oxidative stress. Overall, the authors found that there were hints of efficacy, but it was difficult to say due to number of study quality issues, including widely varying WBC protocols, small sample size, studies that weren't randomized, blinded, or controlled, presence of confounding factors such as diet, physical activity, and lack of proper patient classification, such as stratification by BMI and class of obesity. It is also unclear whether WBC protocols would need to be adjusted for BMI, given that adipose tissue can be a barrier to heat loss and thus could theoretically impact WBC response (Fontana et al., 2022). For instance, a systematic review and meta-analysis by Rymaszewska et al., 2020 looked at the effects of WBC on lipid profiles and reported lower levels of triglycerides after WBC, as well as improvements in levels of total and LDL cholesterol in those with lower BMI. The data they found suggested that lower BMI might predict lipid profile response to WBC. Overall, studies may first need to assess the differential impacts of WBC in those with obesity and potentially change or optimize protocols before being able to determine whether WBC has an effect on weight loss.

Safety: Risks of PBC and WBC can include frostbite, headache, increased blood pressure, and cold panniculitis. Inappropriately administered cryotherapy can increase risks. Many studies do not report adverse events, making it difficult to fully assess safety.

Types of evidence:

- 1 FDA guidance page
- 1 scoping review
- One case report
- 1 conference consensus statement
- 3 reviews
- Information from websites

Unfortunately, WBC studies tend not to actively surveille and/or report potential side effects. There are several reports of frostbite, though this may arise from not following proper protocols such as not entering chambers with wet skin or clothes. Use of any device with liquid nitrogen brings risk of asphyxiation. A scoping review by Legrand et al., 2023, included a review of reported adverse events from 5 case reports and 2 RCTs for a total of approximately 100 participants. The included studies

included primarily middle-aged individuals with conditions like back pain or arthritis. These studies reported 16 total adverse events. Four of these adverse events were serious: global amnesia, cerebral bleeding, a rare cerebrovascular disease called Moyamoya disease, and an aortic dissection. Three of these events occurred immediately after WBC. Minor adverse events included headache, hives, discomfort / dizziness, hypertension, lasting shivering, and panniculitis. Headache was the only adverse event reported twice. The authors examined each case and discussed underlying risk factors or WBC protocols that may have predisposed participants to some of these events and speculate that the risk of adverse events may be mitigated by proper adherence to safety protocols and contraindications. As many trials do not include safety information, there is a concern that adverse events are underreported.

There are several contraindications for cryotherapy: hypertension not controlled by medication, serious coronary or pulmonary disease, arrhythmia, circulatory disorders including peripheral artery occlusive disease and history of deep-vein thrombosis, severe Raynaud's Syndrome, cold allergies, cold-induced bronchial obstruction or other signs of cold allergy, acute renal or urinary disorders, history of seizures, skin infections on a substantive portion of the body, wound-healing problems, and severe anemia (Bad Voslau Consensus; Bleakley et al., 2014). Pregnancy is also typically included as a contraindication, and the Bad Voslau Consensus lists several other relative contraindications including polyneuropathies, hypothyroidism, vasculitis, and hyperhidrosis. Side effects can include local first and second degree frostbite, headaches or exacerbation of pain, increased blood pressure, and cold allergy (Bad Voslau Consensus).

Despite these contraindications, WBC is widely used by the general public.

Drug interactions:

The drug interactions of whole-body cryotherapy have not been delineated. See the Safety section for discussion of contraindicated medical conditions.

Research underway:

There are approximately 90 ongoing trials that involve cryotherapy in some way. Most of these trials are for superficial or targeted cryotherapy, particularly for oncological purposes.

NCT05315011 is an ongoing study on the analgesic effects of whole-body cryotherapy for patients experiencing joint pain while receiving aromatase inhibitor treatment for hormone-dependent breast cancer. The study will randomize 70 patients to either placebo cryotherapy or whole-body cryotherapy. Placebo treatment will entail entering a chamber at -85˚C for 1 minute. Whole-body cryotherapy will involve entering a chamber at -85˚C for 4.5 minutes. All patients will receive daily sessions for 10 total days. The study outcomes will be assessments of pain and function, including change in most intense pain as the primary outcome measure and use of analgesics as a secondary outcome measure.

There is one ongoing study for partial-body cryotherapy as a treatment for fatigue for patients with Multiple Sclerosis (MS) (NCT05219201). The trial aims to enroll 80 individuals with MS during an inpatient or outpatient rehabilitation stay. Patients will be randomized to 15 sessions of either sham treatment at -30˚C or active treatment at -120˚C. Sessions will each be 2-3 minutes long and will occur daily for inpatient participants and during scheduled sessions for outpatient participants. The primary outcome of this study is measures of severity of fatigue syndrome. Secondary outcome measures include assessments of sleep, quality of life, depression, and physical assessments such as endurance and balance.

Search terms:

Pubmed, Google: whole-body cryotherapy, partial body cryotherapy, whole-body cryostimulation, partial body cryostimulation

- Dementia, cognition, clinical trial, safety, pain

Websites visited for whole-body cryotherapy:

- WebMD.com

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