Pain Physician 2025; 28: 11-23 • ISSN 1533-3159

Narrative Review

Optimizing Chronic Pain Treatment: A Summary of Infrequently Investigated Therapeutic Interventions for Modulating Pain

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Disclaimer: There was no external funding in the preparation of this article.

Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article.

Article received: 04-29-2024
Revised article received: 07-11-2024
Accepted for publication: 09-09-2024

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Background: Although chronic pain is generally treated with pharmacological and surgical interventions, many patients still fail to reach adequate pain relief through these methods. Patients and providers have looked to complementary and alternative strategies for managing chronic pain due to these methods' feasibility and cost-effectiveness and patients' preferences for them. Some promising interventions for chronic pain include resistance training, fasting therapy, sauna therapy, and cryotherapy.

Objectives: The purpose of this narrative review is to provide a scoping overview of the mechanisms, efficacy, and applications of infrequently studied interventions for chronic pain disorders.

Study Design: A narrative review of peer-reviewed literature examining the analgesic effects of 1) resistance training, 2) fasting therapy, 3) sauna therapy, and 4) cryotherapy on chronic pain.

Methods: In September 2023, the PubMed, Embase, and Google Scholar databases were reviewed to identify research on the effects of resistance training, fasting therapy, sauna therapy, and cryotherapy on chronic pain. Our selection included randomized control trials, cohort studies, cross-sectional trials, qualitative studies, and review articles.

Results: The mechanisms by which resistance training, fasting therapy, sauna therapy, and cryotherapy contribute to analgesia occur either in isolation or synergistically. The details of these mechanisms have yet to be fully elucidated, but they likely include central processes, peripheral mechanisms, neurotransmitters, nervous system activation, and mood enhancement. These modalities have shown promising results for a variety of chronic pain disorders, such as arthropathies, rheumatoid and rheumatoid-related conditions, and musculoskeletal conditions.

Limitations: This narrative review is not systematic in nature but is instead focused on providing an overview of the effects of the interventions on chronic pain disorders. Some of the studies included in this review are limited by their sample sizes, study periods, and lack of control groups for adequate comparison. Furthermore, many of the chronic pain conditions mentioned in this review lack investigations sufficient to suggest specific recommendation statements.

Conclusions: The experimental evidence that confirms the pain-alleviating properties of these therapeutic modalities is scarce and warrants further investigation. However, a substantial amount of work supports the use of these modalities in the multimodal and multidisciplinary managements of chronic pain disorders. Future work should continue to elucidate the relationships between chronic pain disorders and resistance training, fasting therapy, sauna therapy, and cryotherapy so that guidelines can be developed.

Key words: Chronic pain, complementary therapies, resistance training, exercise, fasting therapy, diet, sauna therapy, heat therapy, cryotherapy, cold water immersion

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Chronic pain is a significant public health issue that affects more than 30% of people worldwide. Clinically, the chronic pain diagnosis refers to any pain that persists for over 3 months due to failed treatment and/or the uncontrolled pathological process causing the pain (1). The Center for Disease Control and Prevention estimates that as many as 40% of U.S. adults (100 million individuals) experience chronic pain (2). The most alarming and problematic aspect of chronic pain is the magnitude of patients who are treated unsuccessfully (3). The National Health Interview Survey 2019 longitudinal cohort trial reported that only 10.4% of people with chronic pain in 2019 were living pain-free lives in 2020 (4), indicating that pain management strategies have been inadequate and leave significant room for improvement.

Traditionally, chronic pain has been treated pharmacologically with nonopioid medications, including nonsteroid anti-inflammatory drugs, muscle relaxants, antidepressants, and gabapentinoids. Minimally invasive interventions (e.g., nerve blocks, injection therapy, radiofrequency ablation, spinal stimulator implants) have also been incorporated into pain management care plans. A report by the US Department of Health and Human Services that outlines important considerations for chronic pain management (5) recommends a multidisciplinary approach, including complementary and alternative strategies (Table 1). In recent years, complementary and alternative approaches to chronic pain management have received newfound interest due to their feasibility, accessibility, cost-effectiveness, and perceived effectiveness as well as chronic pain patients' preferences for them.

Table 1. *Summary of best practices for pain management as reported by the U.S. Department of Health and Human Services.*

Pain Management Best Practices*
An individualized approach to diagnosis and treatment with emphasis on establishing a therapeutic alliance.
Multidisciplinary approach utilizing one or more treatment modalities guided by a biopsychosocial model of care • Medication • Restorative therapy • Interventional approaches • Behavioral approaches • Complementary and integrative approaches†
Consideration for special populations, stigmas, barriers to care, and risk assessment
Provide education to patients, families, caregivers, clinicians, and policymakers about chronic pain and its treatment
Mitigate unnecessary opioid use

*Pain management best practices as stated by a 2019 U.S. Department of Health and Human Services report (5).
†Including resistance training, fasting therapy, sauna therapy, and cryotherapy.

There are several lifestyle interventions that are less frequently reported as therapeutic in the context of chronic pain management, such as resistance training, fasting therapy, sauna therapy, and cryotherapy. These interventions have been utilized by individuals and clinicians in promoting good health, achieving longevity, protecting against disease, and managing chronic conditions. Although these modalities have been around for centuries, some are just beginning to be evaluated in the context of chronic pain management.

The purpose of this review is to provide a narrative overview of the analgesic mechanisms and therapeutic applications of resistance training, fasting therapy, sauna therapy, and cryotherapy in chronic pain management. For each of these interventions, this study will comment on plausible mechanisms that govern its analgesic benefits and follow this commentary with an overview of the most recent literature about the application of the therapy to chronic pain disorders. We hope that this narrative review will provide readers with 1) an overview of the clinical applications and benefits of these adjunctive pain management therapies and 2) an introduction to the analgesic mechanisms reported with these modalities. By addressing these goals, this narrative review will guide understanding of these interventions in the context of chronic pain management.

Methods

Search Strategy

Knowing the scarcity of information available on the aforementioned therapeutic interventions in the context of chronic pain disorders and the variations in how these therapies are implemented, the authors decided that a narrative review would serve readers best and be most suitable for publication (6). We conducted a wide-ranging literature review that addressed the mechanisms and outcomes of these therapeutic interventions in chronic pain disorders. The following search engines and electronic databases were accessed for articles published up to September 2023: MEDLINE (access via PubMed), Embase, and Google Scholar. Using Boolean operators and MeSH terms, we entered the following search terms into each database with various phrase inputs: chronic pain, pain management, pain tolerance, resistance training, exercise therapy, fasting therapy, dietary fasting, heat therapy, sauna therapy, cold therapy, and cryotherapy. All the papers obtained by our search strategy were individually reviewed for their content and relevance to the aims of this review. We also read additional papers that came up as the most relevant in the respective references of the above articles.

Articles that met the inclusion criteria were: (1) randomized controlled trials, observational cohort studies, cross-sectional trials, or qualitative studies that addressed the study aims; (2) original studies or a review articles that provided context for or explanations of the pain-alleviating properties of those therapeutic interventions in chronic pain disorders; (3) accessible in the English language; (4) focused on adult chronic pain populations; and (5) descriptive of relevant outcome measures (e.g., pain severity, pain medication reliance, disease symptomatology, disease-specific activity scores). Articles were excluded if they (1) were not available in the English language; (2) did not report on pain-related parameters; or (3) did not attempt to clearly describe the therapeutic intervention used (e.g., type of exercise training, dietary protocol, heat therapy, or cold therapy).

Results

Resistance Training as an Analgesic Therapy

Resistance training, also known as strength training, is a form of physical activity in which muscle fibers shorten and contract against either a static or dynamic resistance. This mechanical work provides a stimulus to tissues, including skeletal muscle, tendons, ligaments, and bones, causing distinct changes in the functional and architectural properties of the involved structure. Although the origins of the utility of resistance training are deeply rooted in physical performance contexts, the application of this modality has also been extended as a therapeutic intervention for promoting longevity, optimizing health, maintaining psychological well-being, and treating disease. Now, resistance training has been applied for the management of chronic pain disorders (Fig. 1).

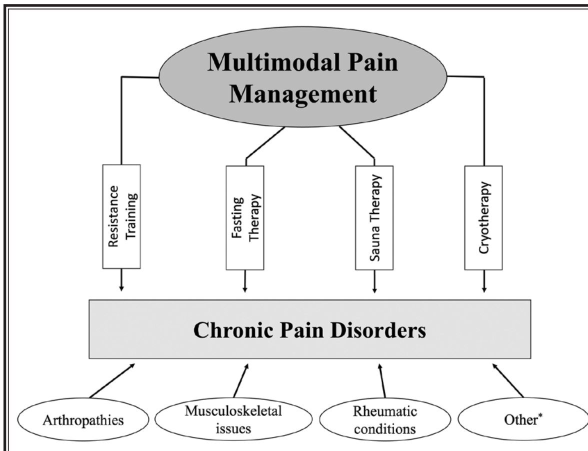

Fig. 1. *Representation of best practices for treating chronic pain disorders with multimodal approaches, which can incorporate complementary therapeutic interventions such as resistance training, fasting therapy, sauna therapy, and cryotherapy. Includes spinal cord injuries, dysmenorrhea, migraine-type headaches, tension-type headaches, chronic fatigue syndrome, and complex regional pain syndrome.*

The mechanisms by which resistance training and all other modalities discussed in this review exert analgesia are not fully understood and are likely multifactorial (Fig. 2). Although the proposed analgesic mechanisms for each modality are, to reiterate, multifactorial, relief from each chronic pain pathology may possibly be achieved through a mechanism that is specific to the disease entity. Experimental trials have demonstrated that neurotransmitters (e.g., beta-endorphin, met-enkephalin, substance P, ATP, cytokines) (7-9), androgen receptor activation (10), the peripheral immune system (11), and central processes are likely implicated during resistance training. A related important consideration is that among chronic pain patients who exercise, improvements in psychological well-being seem to correlate with those in pain tolerance. The benefits of exercise on chronic pain likely have some relationship to the reported improvements in mood, depression, self-image, and behavior that occur with exercise therapies (12). It is impossible to distinguish the relative contributions these factors may have to exercise-induced analgesia in patients with chronic pain disorders. Therefore, the influence of these factors should be considered in the context of the aforementioned biological mechanisms.

Across various activity levels and age groups, patients with a plethora of musculoskeletal pathologies are reported to experience pain alleviation with resistance training. Patients who have chronic low back pain see improvements in pain, quality of life, and pain-related disability (13-15) when the individuals affected by the condition engage in structured resistance training protocols, and this benefit appears to be dose-dependent (16). Similarly, there is substantial evidence

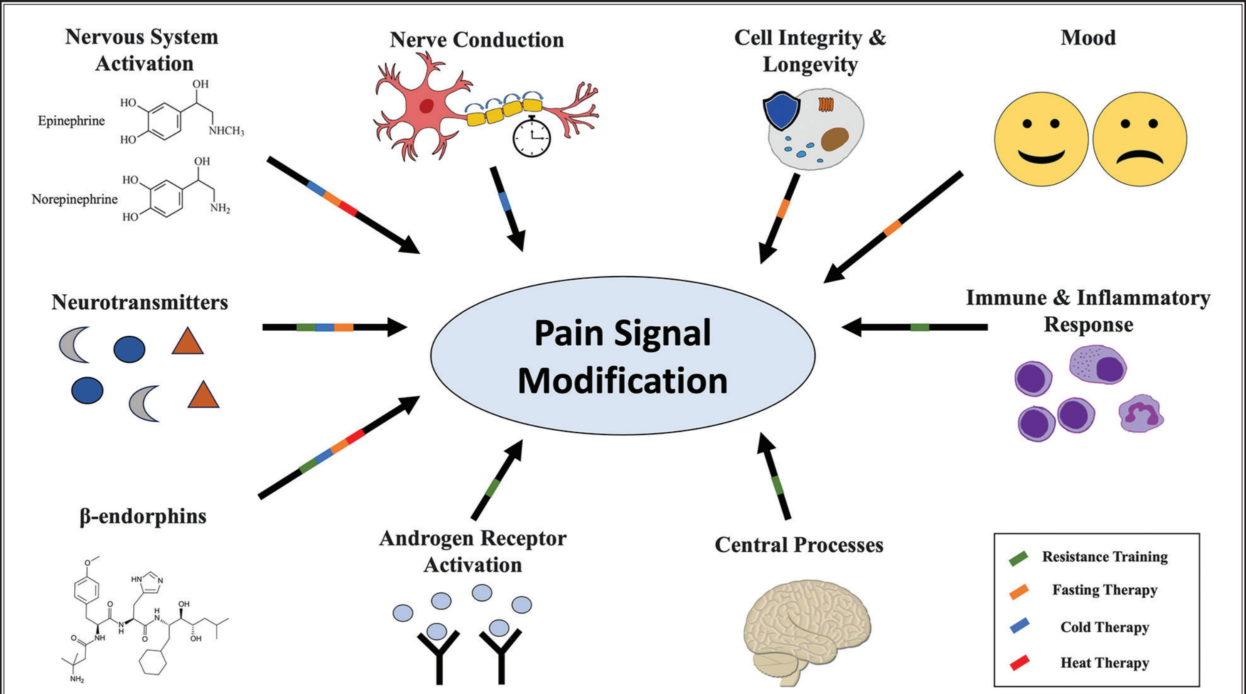

Fig. 2. *Schematic representation of the various pain-signaling mechanisms implicated by resistance training, fasting therapy, sauna therapy, and cryotherapy.*

supporting the analgesic properties of resistance training for persons with chronic ergonomic-related pain, such as pain in the neck (17,18) and upper extremities (19). The most well-established pain-alleviating effect resistance training has on musculoskeletal pathologies is observed in patients with osteoarthritis. Specifically, significant improvements in pain scores have been reported by patients with knee osteoarthritis who engage in structured resistance training regimens across various training designs (e.g., length of training, isometric vs. dynamic resistance training) (20,21). The analgesic benefits conferred by resistance training for these individuals have been well-characterized and summarized in high-quality reviews within the literature (22,23).

The analgesic benefit seen with resistance training also extends to patients with diseases of autoimmune etiology, including fibromyalgia and rheumatoid arthritis. Fibromyalgia and rheumatoid arthritis are chronic pain pathologies studied extensively in the context of resistance training, with a variety of experimental designs, control groups, and concurrent therapies (e.g., aerobic therapy, flexibility training). Despite these experimental variations, resistance training consistently provides analgesic benefits to these patient populations in the form of reductions in pain severity and pain medication reliance (24-29). Notably, while training is no more efficacious in producing analgesia than are other exercise modalities in some trials, these results are still particularly relevant for patients who are unable or unwilling to participate in endurance exercise but wish to obtain pain alleviation.

Finally, resistance training has been investigated for its potential analgesic properties in patients with other chronic pain disorders, including migraine-type headaches (30), spinal cord injuries (31), polymyositis, and dermatomyositis (32). Although less investigated and with studies of much smaller sample sizes, these chronic pain pathologies appear to also be positively affected by resistance training, with studies reporting reduced pain severity and pain symptoms among afflicted individuals.

The effects of resistance training and other exercise therapies on chronic pain have been well summarized by other researchers (23,29,33-40) (Table 2). Overall, when resistance training with appropriate exercise parameters is applied to chronic pain conditions, individuals are likely to experience improvements in pain and pain-related symptoms. For the chronic disease processes described above, the available literature provides no conclusive evidence for which of resistance

Table 2. *Summary of high-quality review articles reporting on the pain-alleviating effects of resistance training on patients with chronic pain disorders.*

Study	Study Type	Intervention	Number of Trials	Chronic Pain Disorders Discussed	Study Goals	Conclusions
Botta et al (40)	Narrative review	Resistance training	8	Fibromyalgia, low back pain, axial, diabetes-related musculoskeletal pain, spondyloarthritis, cancer-treatment induced pain, persistent pain following trauma,	Establish the effects of high-intensity interval-based resistance training (HIIT), used either in isolation or in conjunction with other exercise therapies, on chronic pain conditions	Low-quality evidence supports the analgesic effects of HIIT on chronic pain disorders. More high-evidence trials are needed to strengthen this support.
Busch et al (33)	Cochrane Review	Resistance training	5	Fibromyalgia	Evaluate and potential benefits (e.g., pain relief) or harms associated with resistance training in adult fibromyalgia patients	Moderate- and moderate-to-high-intensity resistance training exercise improved pain in fibromyalgia patients. There was low-quality evidence supporting the superiority of aerobic training to resistance training in alleviating pain. Low-quality evidence also suggested the superiority of resistance training over flexibility training in alleviating pain.
Nelson et al (34)	Literature review	Resistance training	11	Fibromyalgia	Determine if fibromyalgia patients can engage in enough muscle-strengthening activities to obtain pain relief through resistance training	Resistance training-based muscle strengthening was safe and effective in eliciting pain reduction in fibromyalgia patients, especially when the exercise programming progressed from low intensities.
Turner et al (23)	Systematic review	Resistance training	12	Osteoarthritis	Determine if resistance training affects pain tolerance in patients with knee osteoarthritis and report on any dose-response relationships that might exist	Resistance training improves pain perception in patients with knee osteoarthritis. Although the largest effect sizes were observed with trials of at least 24 sessions across 8-12 weeks' duration, no optimal exercise dose (intensity, repetitions, frequency) was found.
Latham et al (22)	Meta-analysis	Resistance training	8	Osteoarthritis	Summarize the potential benefits of progressive resistance training in older adults with osteoarthritis	Resistance training elicited a significant reduction in pain ($MD = -0.35$, 95% CI: -0.52, -0.18, $P < 0.001$). These results indicate that strength training should be utilized by elderly patients with osteoarthritis.
Naugle et al (37)	Meta-analysis	Resistance Training	4	Shoulder myalgia, fibromyalgia	Evaluate the effects of resistance training (e.g., isometric exercise) on exercise-induced hypoalgesia in chronic pain populations	Resistance training reduced pain perception in patients with shoulder myalgia. However, these improvements were not reversed in fibromyalgia patients. Across all chronic pain conditions, the average effect size of isometric resistance training was 0.40 ($SD = 1.43$).
Gross et al (35)	Cochrane review	Various exercise conditions (resistance training, aerobic exercise, flexibility training, mindfulness, feedback exercises)	27	Chronic neck pain	To access the effectiveness of various exercise therapies on pain and other mechanical neck disorder disease parameters	Upper-extremity resistance training had a moderate-to-large positive effect on chronic neck pain that began immediately after the treatment and persisted at the short-term follow-up. The utilization of specific strengthening resistance exercises for chronic neck pain, cervicogenic headache, and radiculopathy may be beneficial, especially in the context of other exercise modalities.

Table 2 cont. *Summary of high-quality review articles reporting on the pain-alleviating effects of resistance training on patients with chronic pain disorders.*

Study	Study Type	Intervention	Number of Trials	Chronic Pain Disorders Discussed	Study Goals	Conclusions
Kroll et al (38)	Narrative review	Various exercise conditions (resistance training, aerobic exercise, flexibility training, movement therapies)	4 (resistance training x pain outcomes)	Fibromyalgia, osteoarthritis, CRPS, low back pain,	Summarize important considerations for exercise therapy in chronic pain patients, including mechanisms, applications, and successful exercise prescription	Exercise therapy is therapeutic for wide-ranging chronic pain disorders, but it is difficult to demonstrate if one exercise modality is superior to others.
Ambrose et al (39)	Narrative review	Various exercise conditions (resistance training, aerobic exercise, flexibility training, movement therapies)	3 (resistance training x pain outcomes)	RA, fibromyalgia	Report on the effects of exercise therapies on chronic pain pathogenesis	Multimodal therapy, including resistance-based exercise therapy, may be most effective for chronic pain management. Treatment success is dependent on considerations of patients' needs, abilities, and interests.
Baillet et al (29)	Meta-analysis	Resistance training	5	RA	Evaluate the efficacy of resistance training on various disease-specific outcomes (e.g., pain)	With resistance training, a trend toward a small positive effect on pain was observed (MD = 4.1 mm, 95% CI: 11.0-2.7 mm, p = 0.24; I2 = 54%, 95% CI: 0-82%). These results are unlikely to be clinically relevant.
Geneen et al (36)	Cochrane review	Various exercise conditions (resistance training, aerobic exercise, flexibility training, movement therapies)	21 reviews with 264 studies	RA, osteoarthritis, fibromyalgia, low back pain, neck pain, dysmenorrhea, spinal cord injury	Qualitative report on effectiveness of different exercise interventions in improving pain severity and other secondary outcomes of chronic pain disorders	Quality of evidence was low due to limited patient follow-up and potentially underpowered studies. Several reviews reported favorable improvements in pain severity. However, these results were inconsistent across multiple exercise interventions and chronic pain disorders. Exercise had a greater impact on physical function and musculoskeletal pain than on pain relief or neuropathic pain. Future research is required and should address the shortcomings of this study's methodology.

HIIT = high-intensity interval training; MD = mean difference; CRPS = complex regional pain syndrome; RA = rheumatoid arthritis; CI = confidence interval

training's analgesic mechanisms govern pain relief. As with the other nonpharmacological therapeutic modalities discussed below, chronic pain pathologies appear to be best used as part of a multimodal approach to pain management.

Analgesic Properties of Fasting Therapy in Chronic Pain Disorders

The dietary restriction of energy consumption despite adequate access to food resources (also known as fasting) is another therapeutic intervention that shows promise as a pain-modulating therapy. During periods of fasting, cellular, genetic, and physiological changes occur that allow the body to switch from a state of energy consumption to a state of energy conservation. As an intervention, fasting therapies have been utilized and investigated in a myriad of clinical diseases. While fasting therapy has been used prophylactically as a modality to protect against the occurrence of disease processes (e.g., metabolic syndrome, diabetes), it has also been used therapeutically as a treatment for ongoing disease states, including chronic pain.

As with resistance training, the mechanisms that govern the clinical health benefits observed with fasting therapies are largely unknown and likely multifactorial. Fasting therapy induces biochemical changes that maintain cell integrity, reduce oxidative stress, and slow cellular aging (41), and these responses in part explain the benefits seen with both pain and non-pain-related processes (e.g., cancer treatment and prevention, endocrine pathologies, autoimmune processes, mood disorders). However, 2 implicated mechanisms are likely to explain the analgesia observed with fasting therapy—the therapy may work indirectly through moodenhancing effects and directly through alterations in pain signaling and perception (41). The pain-processing changes that occur with fasting therapy are linked to neurotransmitters (e.g., endogenous endorphins, neuropeptide Y) (42,43), serotonin availability (44), and ketone bodies (45). It is plausible that the cumulative analgesic effect of these neurotransmitters contributes to pain modulation in the chronic pain pathologies described below. However, conclusions cannot be made as to which of these neurotransmitters bear the greatest importance for each pain process.

Analgesic Properties of Fasting Therapy in Chronic Disease Processes

The chronic pain pathology that has shown the most promising improvements with fasting therapy is rheumatoid arthritis. Numerous randomized control trials have reported improvements in pain scores and pain medication reliance among rheumatoid arthritis patients who complete fasting therapy regimens, supporting the hypothesis that this therapy has analgesic effects on this population (46,47). Case reports in the literature further corroborate these antinociceptive claims (48). The results of additional fasting therapy investigations in rheumatoid arthritis populations have been well summarized (49,50) and further evidence the pain-alleviating properties of this therapeutic modality. The influence of fasting therapy on arthropathies also applies to osteoarthritis of various locations, with studies demonstrating reduced pain severity, decreased pain medication reliance, and improvements in articular function and overall symptomatology (51). Available literature also focuses on the weight-sparing effects of fasting therapy for patients with osteoarthritis and the accompanying pain they perceive. A review by Babu et al states (52) that intermittent fasting should be utilized as a strategy for obese patients with knee osteoarthritis due to the interaction of weight, inflammation, degenerative changes, and pain associated with this pathology.

Chronic fluctuating pain disorders seen most commonly in women, such as fibromyalgia and dysmenorrhea, also appear to benefit from multidisciplinary pain approaches that include the use of fasting therapy. Specifically, these chronic pain pathologies were shown to have significant short-term improvements in pain perception, mood changes, and answers given on disease-specific impact questionnaires (53,54).

The data presented on these chronic pain disorders here and in high-quality reviews on this topic suggest that fasting therapy may have an adjunctive role in treating pain (41,49,50,52). Traditional and integrative treatment strategies utilized for these disorders should consider incorporating fasting therapy when appropriate. The work thus far is promising and highlights the value of this cost-effective, accessible intervention as part of a multimodal approach to pain management.

Sauna Therapy as a Modality for Modifying Pain in Chronic Disease

For over a century, saunas have been used as a therapeutic intervention for maintaining good health and treating a myriad of diseases. Sauna therapy is a type of spa therapy that broadly refers to the application of a significant amount of heat in a fixed environment. This heat application can be coupled with immediate cold-water exposure. Sauna therapy and its physiological and therapeutic effects on the body have been researched extensively, with observations made on how the therapy affects cardiovascular, metabolic, respiratory, hormonal, and nervous-system responses.

The analgesic properties of sauna therapy are likely mediated through increased levels of β-endorphins. Within the literature, consistent increases in β-endorphins after sauna therapy are reported (55,56). Further evidence supporting the causal relationship between sauna therapy and β-endorphin levels comes from experimental trials on chronic drug users. When cocaine addicts were subjected to thermal stress via sauna therapy, they did not achieve observable increases in their adrenocorticotropic hormone/β-endorphin levels (57). This finding indicates that sauna therapy is related to the neuroendocrine control of the pituitary gland and that this relationship is ameliorated when neuroendocrine signaling is disrupted. The direct mechanisms by which sauna therapy elicits changes in β-endorphin levels have not been stated in the literature and warrant investigation. If other mechanisms govern this pain-alleviating benefit, they have yet to be identified or elucidated within the literature.

Sauna therapy has beneficial pain-alleviating effects on rheumatological processes. Numerous investigations into the analgesic properties of sauna therapy on patients with fibromyalgia have been completed, with most showing significant improvements in pain threshold from baseline values (58) that may be present for as long as 6 months after the intervention (59). Pain related to rheumatoid arthritis has been reported to be ameliorated through sauna therapy, as evidenced by marked improvements in pain tolerance upon exposure to heat therapy, with many patients reporting relief upon immediate exposure to said therapy (40% of rheumatoid arthritis patients) and immediately upon post-heat cooling (39%) (60). These analgesic properties appear similar to those observed when this form of therapy is given to patients with ankylosing spondylitis (61). The results of these studies indicate that the analgesic properties of sauna therapy are applicable to patients with rheumatological conditions and should be incorporated into multimodal pain treatment plans for these patients.

Chronic fatigue syndrome's association with pain has also subjected it to investigation with sauna therapy. A case report describes 2 patients with chronic fatigue syndrome who were unsuccessful in treating their symptoms with prednisone therapy and sought alternative treatment methods (62). In as few as 15 to 25 daily sessions during an inpatient stay, these patients reported a dramatic improvement in their pain symptoms, demonstrating the potential analgesic effects of sauna therapy in this pathological process. Another report in the literature of 11 patients with chronic fatigue syndrome yielded similar improvements in pain in response to sauna therapy (63). These pain-alleviating findings are also appreciable in the context of other chronic pain disorders, including chronic tension-type headaches (64) and type II diabetes mellitus (65). Significant improvements in pain scores and quality-of-life measures were observed in patients with these conditions.

The efficacy of sauna therapy as part of a multidisciplinary inpatient treatment plan has been evaluated in individuals who have experienced chronic pain for over 6 months (66). When patients participated in sauna therapy in conjunction with rehabilitative modalities, said patients experienced significantly greater improvements in pain-related behavior. A remarkable finding from this study showed that at a 2-year follow-up, 77% of patients who received sauna therapy returned to work, compared to 50% of patients in the control group. These results indicate that although a multimodal approach to managing chronic pain is beneficial and should be employed, sauna therapy appears to confer benefits that adjunctively further improve pain tolerance. The findings provide additional evidence of the importance of multimodal approaches to pain management and the inclusion of complementary therapies as part of this strategy.

The evidence shown by these studies demonstrates the clinical utility of sauna therapy as a therapeutic modality for various chronic pain disorders. Review articles on sauna therapies further establish the role of this intervention in chronic pain disorders (67). While more work is needed to determine the analgesic action of sauna therapy, this pathway likely largely involves β-endorphins for all the described chronic pain processes. Given the advantageous risk-to-reward ratio of sauna therapy, patients with chronic pain disorders should currently consider incorporating this therapy as an adjunctive treatment for their pain.

Cryotherapy Reduces the Chronic Pain Burden in Distinct Disease Processes

Of the complementary pain management modalities discussed in this review, cold therapy has the longest-standing history, originating as long ago as 3,500 B.C. (68). Since then, cold therapies have been utilized for treating a myriad of physical conditions both related and unrelated to chronic pain. In recent literature, cold therapy has become synonymous with cryotherapy, an umbrella term that encompasses varying methods of inducing physiological temperature reductions, including cold-water immersion, whole-body cooling, and ice therapy (69). Although these methods vary in their modes of cold transmission, exposure times, required apparatuses, and cooling efficiencies, they collectively enact a cascade of physiological changes that have been used prophylactically and therapeutically to adjunctively treat acute and chronic forms of a plethora of pain conditions.

Cryotherapies induce a cascade of physiological changes that may account for the modalities' analgesic properties either separately or synergistically. There are prominent alterations to blood flow patterns and inflammatory pathways that contribute in part to pain alleviation. Specifically, an anti-inflammatory state is promoted through microvascular vasoconstriction, the slowing of metabolic processes, the mitigation of inflammatory cytokine and myokine responses, and the dampening of inflammatory signals. However, the precise mechanism by which cryotherapies induce analgesia is multifactorial, with contributions likely coming from reduced nerve conduction velocity, closed pain gates (see the pain gate theory), nociceptor inhibition, reduced skeletal muscle activity, and diminishment of the activity of metabolic enzymes (70-72). Hormones also appear to influence cryotherapy-related pain processing, with both attenuated histamine responses (73) and elevated norepinephrine levels (74) observed after repetitive cold exposure therapies. The likeliest contributing mechanism is the inhibition of the descending central nervous system via the release of β-endorphins, since this finding has been observed in multiple cryotherapy investigations (69). Although any one of the chronic pain pathologies described below may be affected by one or multiple analgesic properties, more work is needed to improve our understanding of these relationships.

Within the literature, cryotherapy has been shown to reduce the pain burden in chronic pain disease processes. These cooling strategies offer analgesic benefits to patients with a variety of chronic pain pathologies of musculoskeletal etiology, including chronic low back pain. Specifically, individuals with chronic low back pain are reported to experience significant improvements in their pain scores (75,76) after as few as 4 cryotherapy sessions (77). Similar benefits are conferred to subjects with arthropathies. When used for treating osteoarthritis, cryotherapies are reported to significantly reduce both pain scores and pain medication reliance across multiple cryotherapy regimens (78,79). Cryotherapy was not only effective in reducing the pain associated with those arthropathies but also in decreasing the synovial levels of pro-inflammatory mediators (80), including prostaglandin-E2, nuclear factor kappa B, interleukin-6, interleukin-1β, and vascular endothelial growth factor. Similar investigations have been applied to other inflammatory arthropathies, including gout. Randomized control trials in the literature demonstrate evidence of pain score improvements in gout patients after as little as one week of a cryotherapy intervention (81,82). Another arthropathy that appears to benefit from cryotherapy is rheumatoid arthritis, with many studies reporting significant improvements in patients' pain scores across multiple cryotherapy methods (83,84). Notably, these analgesic benefits persisted for up to 3 months when used in conjunction with traditional multimodal therapy (85). Although these trials present consistent findings, future investigations are warranted, since more evidence is needed to support the interpretation that cryotherapy has analgesic properties in the multimodal management of arthritic pain.

The application of ice therapy may also be applicable to rheumatic diseases, including fibromyalgia, ankylosing spondylitis, and psoriatic arthritis. Analgesia is reported to persist for up to 24 hours after cryotherapy in fibromyalgia patients (86). Patients with ankylosing spondylitis are reported to experience similar pain alleviation, which is evidenced by the reports of dramatic reductions in pain intensity when cryotherapy is used in conjunction with kinesiotherapy (87). A study by Metzger et al (88) evaluating the analgesic effects of cryotherapy on patients with chronic pain caused by various rheumatic pathologies (fibromyalgia, ankylosing spondylitis, and RA) found significant improvements in pain that lasted for up to 90 minutes after therapy. Lastly, the literature also provides a case report of a single patient with psoriatic arthritis (89) who completed 13 sessions of whole-body cooling and experienced an objective improvement in pain perception.

Overall, the evidence provided here shows potential for cryotherapy's ability to exert significant clinical analgesic effects in diseases that are degenerative and rheumatic. Cryotherapy appears to have value when incorporated as part of multimodal pain management plans for the chronic pain disorders discussed here. Cryotherapies demonstrate promise due to their feasibility of completion (cold-water immersion, ice therapy), their ease of access, their minimal medical input, and their cost-effective value.

Discussion

Resistance training, fasting therapy, cryotherapy, and sauna therapy function as significant tools of the management of chronic pain disorders because these therapies modulate pain signaling and subsequently promote pain tolerance. These analgesic properties are mediated by an abundance of mechanisms, which include neurotransmitters (e.g., β-endorphins, serotonin, endocannabinoids), hormones (e.g., norepinephrine), central modulation, the immune system, cellular adaptations, and neuronal alterations. Enhanced psychological well-being also plays a role, and there may be a myriad of mechanisms yet to be fully elucidated. The aforementioned therapeutic interventions act on various points within pain-signaling pathways and are likely to induce pain tolerance separately or synergistically. The experimental evidence that confirms the contributions of these mechanisms is scarce and warrants further investigation. Such investigations should focus on the relative contributions of these mechanisms to pain tolerance in addition to prioritizing the discovery of mechanisms yet to be considered.

The therapeutic modalities discussed here have been applied uniquely to various chronic pain disorders. These therapies appear to have influence on the management of the chronic pain involved in arthropathies (e.g., osteoarthritis, gout), rheumatoid and rheumatoid-related conditions (e.g., rheumatoid arthritis, fibromyalgia, ankylosing spondylitis), spinal cord injuries, chronic headaches (e.g., migraines and tension-types), diabetes, and musculoskeletal conditions (e.g., chronic low back pain, chronic neck pain). Although these individual therapies may vary in the magnitude of their effects on these chronic pain disorders, the experimental and anecdotal evidence provided here suggest that the therapies may alleviate the burden of chronic pain when incorporated into multimodal approaches to management. While some therapeutic interventions and chronic pain disorders have received significant attention (e.g., resistance training, cryotherapy, rheumatoid arthritis, osteoarthritis, fibromyalgia), a paucity of information exists about others (e.g., fasting therapy, sauna therapy, spinal cord injuries, diabetes, ankylosing spondylitis).

The utility of resistance training, fasting therapy, cryotherapy, and sauna therapy in chronic pain management are related to the minimal medical input required. These noninvasive, nonpharmacological interventions require minimal medical supplies and offer cost-effective support in our global fight against economically straining chronic pain disorders. However, it should be noted that not all these methods are without barrier. Some therapies (e.g., whole-body cryotherapy, dietary counseling, access to sauna therapy facilities, personal training) may be difficult to obtain for patients who have trouble obtaining coverage for reasons involving insurance company policies, the need to prove medical necessity, provider qualifications, or reimbursement issues.

These therapeutic modalities should not be used in isolation. Rather, they should serve a complementary role in multidisciplinary and multimodal pain management protocols. Future work should focus on determining which therapies can be used concurrently to optimize pain relief. Patients should consult with their providers on the safety and feasibility of these modalities in their plans for chronic pain management.

Authors' Contributions

AJO carried out the literature search and drafted the first version of the manuscript. MS proposed the idea for the manuscript, provided input for writing, revised the manuscript, and supervised all parts of the process. KG and JS edited and revised the manuscript. All authors read and approved the final version of the manuscript.

References

1. Chandler III G, Rojas AM, Worts PR, Flynn HA. Utilizing multidisciplinary medicine in pain management: A narrative review. *Pain Physician* 2021; 24:369-378.
2. Dahlhamer J, Lucas J, Zelaya C, et al. Prevalence of chronic pain and high-impact chronic pain among adults - United States, 2016. *MMWR Morb Mortal Wkly Rep* 2018; 67:1001-1006.
3. Elliott AM, Smith BH, Hannaford PC, Smith WC, Chambers WA. The course of chronic pain in the community: Results of a 4-year follow-up study. *Pain* 2002; 99:299-307.
4. Nahin RL, Feinberg T, Kapos FP, Terman GW. Estimated rates of incident and persistent chronic pain among US adults, 2019-2020. *JAMA Network Open* 2023; 6:e2313563.
5. US Department of Health and Human Services. Pain Management Best Practices Inter-Agency Task Force report: Updates, gaps, inconsistencies, and recommendations. Published May 6, 2019. https://www.hhs.gov/sites/default/files/pain-mgmt-best-practices-draft-final-report-05062019.pdf
6. Baethge C, Goldbeck-Wood S, Mertens S. SANRA—a scale for the quality assessment of narrative review articles. *Res Integr Peer Rev* 2019; 4:5.
7. Stagg NJ, Mata HP, Ibrahim MM, et al. Regular exercise reverses sensory hypersensitivity in a rat neuropathic pain model: Role of endogenous opioids. *Anesthesiology* 2011; 114:940-948.
8. Chen YW, Tzeng JI, Lin MF, Hung CH, Wang JJ. Forced treadmill running suppresses postincisional pain and inhibits upregulation of substance P and cytokines in rat dorsal root ganglion. *J Pain* 2014; 15:827-834.
9. Martins DF, Mazzardo-Martins L, Soldi F, Stramosk J, Piovezan AP, Santos AR. High-intensity swimming exercise reduces neuropathic pain in an animal model of complex regional pain syndrome type I: Evidence for a role of the adenosinergic system. *Neuroscience* 2013; 234:69-76.
10. Lesnak JB, Fahrion A, Helton A, et al. Resistance training protects against muscle pain through activation of androgen receptors in male and female mice. *Pain* 2022; 163:1879-1891.
11. Lesnak JB, Berardi G, Sluka KA. Influence of routine exercise on the peripheral immune system to prevent and alleviate pain. *Neurobiol Pain* 2023; 13:100126.
12. Mior S. Exercise in the treatment of chronic pain. *Clin J Pain* 2001; 17:77-85.
13. Jackson JK, Shepherd TR, Kell RT. The influence of periodized resistance training on recreationally active males with chronic nonspecific low back pain. *J Strength Cond Res* 2011; 25:242-251.
14. Cortell-Tormo JM, Sánchez PT, Chulvi-Medrano I, et al. Effects of functional resistance training on fitness and quality of life in females with chronic nonspecific low-back pain. *J Back Musculoskelet Rehabil* 2018; 31:95-105.
15. Tjøsvoll SO, Mork PJ, Iversen VM, Rise MB, Fimland MS. Periodized resistance training for persistent non-specific low back pain: A mixed methods feasibility study. *BMC Sports Sci Med Rehabil* 2020; 12:30.
16. Pedersen MT, Andersen LL, Jørgensen MB, Søgaard K, Sjøgaard G. Effect of specific resistance training on musculoskeletal pain symptoms: Dose-response relationship. *J Strength Cond Res* 2013; 27:229-235.
17. Lidegaard M, Jensen RB, Andersen CH, et al. Effect of brief daily resistance training on occupational neck/shoulder muscle activity in office workers with

chronic pain: Randomized controlled trial. *Biomed Res Int* 2013; 2013:262386.

18. Iversen VM, Vasseljen O, Mork PJ, Fimland MS. Resistance training vs general physical exercise in multidisciplinary rehabilitation of chronic neck pain: A randomized controlled trial. *J Rehabil Med* 2018; 50:743-750.
19. Sundstrup E, Jakobsen MD, Andersen CH, et al. Effect of two contrasting interventions on upper limb chronic pain and disability: a randomized controlled trial. *Pain Physician* 2014; 17:145-154.
20. Schilke JM, Johnson GO, Housh TJ, O'Dell JR. Effects of muscle-strength training on the functional status of patients with osteoarthritis of the knee joint. *Nurs Res* 1996; 45:68-72.
21. Topp R, Woolley S, Hornyak J, Khuder S, Kahaleh B. The effect of dynamic versus isometric resistance training on pain and functioning among adults with osteoarthritis of the knee. *Arch Phys Med Rehabil* 2002; 83:1187-1195.
22. Latham N, Liu CJ. Strength training in older adults: The benefits for osteoarthritis. *Clin Geriatr Med* 2010; 26:445-459.
23. Turner MN, Hernandez DO, Cade W, Emerson CP, Reynolds JM, Best TM. The role of resistance training dosing on pain and physical function in individuals with knee osteoarthritis: A systematic review. *Sports Health* 2020; 12:200-206.
24. Kayo AH, Peccin MS, Sanches CM, Trevisani VFM. Effectiveness of physical activity in reducing pain in patients with fibromyalgia: A blinded randomized clinical trial. *Rheumatol Int* 2012; 32:2285-2292.
25. Hooten WM, Qu W, Townsend CO, Judd JW. Effects of strength vs aerobic exercise on pain severity in adults with fibromyalgia: A randomized equivalence trial. *PAIN* 2012;153:915-923.
26. Valkeinen H, Alén M, Häkkinen A, Hannonen P, Kukkonen-Harjula K, Häkkinen K. Effects of concurrent strength and endurance training on physical fitness and symptoms in postmenopausal women with fibromyalgia: A randomized controlled trial. *Arch Phys Med Rehabil* 2008; 89:1660-1666.
27. Gavi MB, Vassalo DV, Amaral FT, et al. Strengthening exercises improve symptoms and quality of life but do not change autonomic modulation in fibromyalgia: A randomized clinical trial. *PLoS One* 2014; 9:e90767.
28. Häkkinen A, Sokka T, Hannonen P. A home-based two-year strength training period in early rheumatoid arthritis led to good long-term compliance: A five-year followup. *Arthritis Rheum* 2004; 51:56-62.
29. Baillet A, Vaillant M, Guinot M, Juvin R, Gaudin P. Efficacy of resistance exercises in rheumatoid arthritis: meta-analysis of randomized controlled trials. *Rheumatology (Oxford)* 2012; 51:519-527.
30. Sari Aslani P, Hassanpour M, Razi O, Knechtle B, Parnow A. Resistance training reduces pain indices and improves quality of life and body strength in women with migraine disorders. *Sport Sci Health* 2022; 18:433-443.
31. Nash MS, van de Ven I, van Elk N, Johnson BM. Effects of circuit resistance training on fitness attributes and upper-extremity pain in middle-aged men with paraplegia. *Arch Phys Med Rehabil* 2007; 88:70-75.
32. Alexanderson H, Dastmalchi M, Esbjörnsson-Liljedahl M, Opava CH, Lundberg IE. Benefits of intensive resistance training in patients with chronic polymyositis or dermatomyositis. Arthritis Rheum 2007; 57:768-777.
33. Busch AJ, Webber SC, Richards RS, et al. Resistance exercise training for fibromyalgia. *Cochrane Database Syst Rev* 2013; 2013:CD010884.
34. Nelson NL. Muscle strengthening activities and fibromyalgia: A review of pain and strength outcomes. *J Bodyw Mov Ther* 2015; 19:370-376.
35. Gross A, Kay TM, Paquin JP, et al. Exercises for mechanical neck disorders. *Cochrane Database Syst Rev* 2015; 1:CD004250.
36. Geneen LJ, Moore RA, Clarke C, Martin D, Colvin LA, Smith BH. Physical activity and exercise for chronic pain in adults: An overview of Cochrane Reviews. *Cochrane Database Syst Rev* 2017; 1:CD011279.
37. Naugle KM, Fillingim RB, Riley JL 3rd. A meta-analytic review of the hypoalgesic effects of exercise. *J Pain* 2012; 13:1139-1150.
38. Kroll HR. Exercise therapy for chronic pain. *Phys Med Rehabil Clin N Am* 2015; 26:263-281.
39. Ambrose KR, Golightly YM. Physical exercise as non-pharmacological treatment of chronic pain: Why and when. *Best Pract Res Clin Rheumatol* 2015; 29:120-130.
40. Botta RM, Palermi S, Tarantino D. High-intensity interval training for chronic pain conditions: A narrative review. *J Exerc Rehabil* 2022; 18:10-19.
41. Michalsen A, Li C. Fasting therapy for treating and preventing disease - current state of evidence. *Forsch Komplementmed.* 2013; 20:444-453.
42. Komaki G, Tamai H, Sumioki H, et al. Plasma beta-endorphin during fasting in man. *Horm Res* 1990; 33:239-243.
43. Silverstein JT, Breininger J, Baskin DG, Plisetskaya EM. Neuropeptide Y-like gene expression in the salmon brain increases with fasting. *General and Comparative Endocrinology* 1998; 110:157-165.
44. Kantak KM, Wayner MJ, Stein JM. Effects of various periods of food deprivation on serotonin turnover in the lateral hypothalamus. *Pharmacol Biochem Behav* 1978; 9:529-534.
45. Field R, Pourkazemi F, Rooney K. Effects of a low-carbohydrate ketogenic diet on reported pain, blood biomarkers and quality of life in patients with chronic pain: A pilot randomized clinical trial. *Pain Med* 2022; 23:326-338.
46. Kjeldsen-Kragh J, Haugen M, Borchgrevink CF, et al. Controlled trial of fasting and one-year vegetarian diet in rheumatoid arthritis. *Lancet* 1991; 338:899-902.
47. Sköldstam L, Larsson L, Lindström FD. Effect of fasting and lactovegetarian diet on rheumatoid arthritis. *Scand J Rheumatol* 1979; 8:249-255.
48. Hartmann AM, Karberg K, Kessler CS. Benefits from a plant-based diet, intermittent fasting and aspects of ayurvedic nutrition in rheumatoid arthritis – a case report. *AIMED* 2023; 10:107-112.
49. Müller H, de Toledo FW, Resch KL. Fasting followed by vegetarian diet in patients with rheumatoid arthritis: a systematic review. *Scand J Rheumatol* 2001; 30:1-10.
50. Chen L, Michalsen A. Management of chronic pain using complementary and integrative medicine. *BMJ* 2017; 357:j1284.
51. Koppold DA, Kandil FI, Güttler O, et al. Effects of prolonged fasting during inpatient multimodal treatment on pain and functional parameters in knee and hip osteoarthritis: A prospective exploratory observational study. *Nutrients* 2023; 15:2695.
52. Babu S, Vaish A, Vaishya R, Agarwal A.

Can intermittent fasting be helpful for knee osteoarthritis? *J Clin Orthop Trauma* 2021; 16:70-74.

53. Michalsen A, Li C, Kaiser K, et al. In-patient treatment of fibromyalgia: A controlled nonrandomized comparison of conventional medicine versus integrative medicine including fasting therapy. *Evid Based Complement Alternat Med* 2013; 2013:908610.
54. Tewani S, Sharma H, Tewani GR, Kodali PB, Nair PM. The long-term impact of therapeutic fasting on primary dysmenorrhea in young female adults: A randomized controlled trial. *Cureus* 2023; 15:e41437.
55. Kukkonen-Harjula K, Oja P, Laustiola K, et al. Haemodynamic and hormonal responses to heat exposure in a Finnish sauna bath. *Eur J Appl Physiol Occup Physiol* 1989; 58:543-550.
56. Kauppinen K, Pajari-Backas M, Volin P, Vakkuri O. Some endocrine responses to sauna, shower and ice water immersion. *Arctic Med Res* 1989; 48:131-139.
57. Vescovi PP, Coiro V, Volpi R, Giannini A, Passeri M. Hyperthermia in sauna is unable to increase the plasma levels of ACTH/cortisol, beta-endorphin and prolactin in cocaine addicts. *J Endocrinol Invest* 1992; 15:671-675.
58. Dönmez A, Karagülle MZ, Tercan N, et al. Spa therapy in fibromyalgia: A randomised controlled clinic study. *Rheumatol Int* 2005; 26:168-172.
59. Matsumoto S, Shimodozono M, Etoh S, Miyata R, Kawahira K. Effects of thermal therapy combining sauna therapy and underwater exercise in patients with fibromyalgia. *Complement Ther Clin Pract* 2011; 17:162-166.
60. Nurmikko T, Hietaharju A. Effect of exposure to sauna heat on neuropathic and rheumatoid pain. *Pain* 1992; 49:43-51.
61. Fioravanti A, Cantarini L, Guidelli GM, Galeazzi M. Mechanisms of action of spa therapies in rheumatic diseases: What scientific evidence is there? *Rheumatol Int* 2011; 31:1-8.
62. Masuda A, Kihara T, Fukudome T, Shinsato T, Minagoe S, Tei C. The effects of repeated thermal therapy for two patients with chronic fatigue syndrome. *J Psychosom Res* 2005; 58:383-387.
63. Masuda A, Munemoto T, Tei C. A new treatment: Thermal therapy for chronic fatigue syndrome. *Nihon Rinsho* 2007; 65:1093-1098.
64. Kanji G, Weatherall M, Peter R, Purdie G, Page R. Efficacy of regular sauna bathing for chronic tension-type headache: A randomized controlled study. *J Altern Complement Med* 2015; 21:103-109.
65. Beever R. The effects of repeated thermal therapy on quality of life in patients with type II diabetes mellitus. *J Altern Complement Med* 2010; 16:677-681.
66. Masuda A, Koga Y, Hattanmaru M, Minagoe S, Tei C. The effects of repeated thermal therapy for patients with chronic pain. *Psychother Psychosom* 2005; 74:288-294.
67. O'Hara E, Babione J. Sauna as a rehabilitative component in chronic pain: A systematic review. *Arch Phys Med Rehabil* 2017; 98:e107.
68. Wang H, Olivero W, Wang D, Lanzino G. Cold as a therapeutic agent. *Acta Neurochir (Wien)* 2006; 148:565-570.
69. Allan R, Malone J, Alexander J, et al. Cold for centuries: A brief history of cryotherapies to improve health, injury and post-exercise recovery. *Eur J Appl Physiol* 2022; 122:1153-1162.
70. Wahren LK, Torebjörk E, Jörum E. Central suppression of cold-induced C fibre pain by myelinated fibre input. *Pain* 1989; 38:313-319.
71. Saeki Y. Effect of local application of cold or heat for relief of pricking pain. *Nurs Health Sci* 2002; 4:97-105.
72. Algafly AA, George KP. The effect of cryotherapy on nerve conduction velocity, pain threshold and pain tolerance. *Br J Sports Med* 2007; 41:365-369.
73. Wojtecka-Lukasik E, Ksiezopolska-Orlowska K, Gaszewska E, et al. Cryotherapy decreases histamine levels in the blood of patients with rheumatoid arthritis. *Inflamm Res* 2010; 59:S253-255.
74. Leppäluoto J, Westerlund T, Huttunen P, et al. Effects of long-term whole-body cold exposures on plasma concentrations of ACTH, beta-endorphin, cortisol, catecholamines and cytokines in healthy females. *Scand J Clin Lab Invest* 2008; 68:145-153.
75. Nugraha B, Günther JT, Rawert H, Siegert R, Gutenbrunner C. Effects of whole body cryo-chamber therapy on pain in patients with chronic low back pain: A prospective double blind randomised controlled trial. *Eur J Phys Rehabil Med* 2015; 51:143-148.
76. Giemza C, Matczak-Giemza M, Ostrowska B, Bieć E, Doliński M. Effect of cryotherapy on the lumbar spine in elderly men with back pain. *The Aging Male* 2014; 17:183-188.
77. Salas-Fraire O, Rivera-Pérez JA, Guevara-Neri NP, et al. Efficacy of whole-body cryotherapy in the treatment of chronic low back pain: Quasi-experimental study. *Journal of Orthopaedic Science* 2023; 28:112-116.
78. Chruściak T. Subjective evaluation of the effectiveness of whole-body cryotherapy in patients with osteoarthritis. *Reumatologia* 2016; 54:291-295.
79. Barłowska-Trybulec M, Zawojska K, Szklarczyk J, Góralska M. Effect of whole body cryotherapy on low back pain and release of endorphins and stress hormones in patients with lumbar spine osteoarthritis. *Reumatologia* 2022; 60:247-251.
80. Guillot X, Tordi N, Laheurte C, et al. Local ice cryotherapy decreases synovial interleukin 6, interleukin 1β, vascular endothelial growth factor, prostaglandin-E2, and nuclear factor kappa B p65 in human knee arthritis: A controlled study. *Arthritis Res Ther* 2019; 21:180.
81. Kurniasari MD, Monsen KA, Weng SF, Yang CY, Tsai HT. Cold water immersion directly and mediated by alleviated pain to promote quality of life in Indonesian with gout arthritis: A community-based randomized controlled trial. *Biol Res Nurs* 2022; 24:245-258.
82. Schlesinger N, Detry MA, Holland BK, et al. Local ice therapy during bouts of acute gouty arthritis. *J Rheumatol* 2002; 29:331-334.
83. Laktašić Žerjavić N, Hrkić E, Žagar I, et al. Local cryotherapy, comparison of cold air and ice massage on pain and handgrip strength in patients with rheumatoid arthritis. *Psychiatr Danub* 2021; 33:757-761.
84. Hirvonen HE, Mikkelsson MK, Kautiainen H, Pohjolainen TH, Leirisalo-Repo M. Effectiveness of different cryotherapies on pain and disease activity in active rheumatoid arthritis. A randomised single blinded controlled trial. *Clin Exp Rheumatol* 2006; 24:295-301.
85. Księżopolska-Orłowska K, Pacholec A, Jędryka-Góral A, et al. Complex rehabilitation and the clinical condition of working rheumatoid arthritis patients: Does cryotherapy always overtop traditional rehabilitation? *Disabil Rehabil* 2016; 38:1034-1040.
86. Samborski W, Stratz T, Sobieska M, Mennet P, Müller W, Schulte-Mönting J. Intraindividual comparison of

whole body cold therapy and warm treatment with hot packs in generalized tendomyopathy. *Z Rheumatol* 1992; 51:25-30.

87. Stanek A, Cholewka A, Gadula J, Drzazga Z, Sieron A, Sieron-Stoltny K. Can whole-Body cryotherapy with subsequent kinesiotherapy procedures in closed type cryogenic chamber improve BASDAI, BASFI, and some spine mobility parameters and decrease pain intensity in patients with ankylosing spondylitis? *Biomed Res Int* 2015; 2015:404259.
88. Metzger D, Zwingmann C, Protz W, Jäckel WH. Whole-body cryotherapy in rehabilitation of patients with rheumatoid diseases--pilot study. *Rehabilitation (Stuttg)* 2000; 39:93-100.
89. Leone R. Reduction of pain in PsA (psoriatic arthritis) with WBC treatment: Changing quality of life. *J Clin Rheumatol Arthritis* 2023; 1:1-5.