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Thermal Therapies and Peptide Signaling in Women's Health: A Systems-Based Review

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Abstract

Background: Cold water immersion (CWI), sauna bathing, and peptide-based interventions are increasingly used to support recovery, cardiometabolic health, and overall well-being among women. Despite widespread adoption, the evidence base—particularly in female populations—remains heterogeneous, shaped by sex-specific differences in thermoregulation, hormonal physiology, and autonomic responsiveness. Objective: This narrative review synthesizes current clinical and mechanistic evidence across these three modalities, with emphasis on female-specific physiological pathways, hormonal interactions, and translational health outcomes. Methods: Relevant literature was identified through searches of PubMed, Scopus, and Web of Science, with an emphasis on studies published from 2015 to 2025 and supplemented by landmark earlier work where appropriate. Results: Sauna bathing demonstrates the most robust evidence base, with dose-dependent reductions in cardiovascular mortality and improvements in endothelial function mediated by heat shock protein upregulation, nitric oxide synthase activation, and autonomic modulation. Cold water immersion shows moderate evidence for exercise recovery and emerging data on brown adipose tissue activation and hormesis-driven metabolic adaptation, though female-specific protocols remain understudied. Peptide therapies span a broad spectrum: GLP-1 receptor agonists are clinically validated for metabolic and cardiovascular outcomes; collagen peptides show evidence for musculoskeletal support; and experimental compounds such as BPC-157 and mitochondrial peptides demonstrate mechanistic promise but lack human clinical trial data. All three modalities converge on shared physiological pathways including autonomic regulation, mitochondrial adaptation, vascular remodeling, and cellular stress signaling. Conclusion: These approaches represent a complementary systems-based framework for women's health, particularly during the perimenopausal and

postmenopausal transitions. Female-specific clinical trials and standardized protocols are urgently needed to advance translational application.

Keywords

Cold Water Immersion, Sauna Bathing, Peptide Therapy, Women's Health, Menopause, Thermoregulation, Systems Biology

1. Introduction

Cold water immersion and sauna bathing have re-emerged as prominent interventions in both clinical and performance settings, moving from traditional cultural practices into mainstream wellness and integrative medicine. Sauna bathing has roots in Finnish culture spanning thousands of years, while cold water therapy has been documented in ancient Greek, Roman, and Japanese traditions. In recent decades, modern scientific inquiry has begun to rigorously characterize the physiological mechanisms underlying these therapies, generating a rapidly expanding literature that spans exercise physiology, cardiovascular medicine, and endocrinology. Peptide-based therapies represent a parallel and rapidly evolving domain, encompassing molecules that function as endogenous signaling agents capable of modulating metabolism, inflammation, hormonal balance, and tissue repair at the cellular level [1]. The convergence of these three modalities within a systems-biology framework offers a compelling opportunity to rethink integrative approaches to women's health.

A critical limitation of the existing evidence base is the historic underrepresentation of women in thermal therapy and exercise physiology research. The majority of foundational studies on cold water immersion and sauna bathing were conducted in male cohorts, predominantly middle-aged Scandinavian men, and caution is therefore warranted when extrapolating findings to women [2]. Women differ from men in several physiologically meaningful ways relevant to these interventions: they exhibit lower basal metabolic rates, higher body fat percentages, different patterns of fat distribution, and distinct thermoregulatory dynamics influenced by estrogen and progesterone fluctuations across the menstrual cycle [3]. Estrogen, for example, augments peripheral vasodilation by directly influencing vascular smooth muscle and endothelial nitric oxide synthase activity, which alters the hemodynamic response to both heat and cold stress compared to male physiology [4]. These differences are not merely quantitative; they represent qualitatively distinct physiological responses that demand female-specific investigation.

The relevance of these interventions is heightened across key female life stages, including the reproductive years, perimenopause, and postmenopause, each characterized by shifting hormonal landscapes that influence cardiometabolic risk, inflammatory tone, musculoskeletal integrity, and psychological well-being. The

perimenopausal transition, in particular, is associated with accelerating declines in estrogen that drive increases in central adiposity, insulin resistance, vascular stiffness, and bone resorption which are all domains in which thermal therapies and peptide signaling have mechanistic relevance [2]. This review therefore adopts a life-stage perspective, examining the evidence for CWI, sauna bathing, and peptide interventions with explicit attention to female-specific outcomes, mechanistic pathways, and clinical applicability. Where female-specific data are unavailable, extrapolations from mixed-sex or male cohorts are presented with appropriate caveats, and gaps in the literature are identified as priorities for future research.

For the purposes of this review, a systems-based framework is defined as the evaluation of these interventions according to their convergent effects on shared physiological networks—autonomic, vascular, mitochondrial, and inflammatory—rather than as isolated actions on separate organ systems, and this framework is used throughout to compare the relative strength of evidence and mechanistic contribution of sauna bathing, cold water immersion, and peptide therapy across the female lifespan. Table 1 summarizes this convergence model, outlining the shared physiological pathways through which cold water immersion, sauna bathing, and peptide signaling intersect and the downstream outcomes relevant to women's health.

Table 1. Mechanism model of thermal stress and peptide signaling in women's health.

Pathway	Cold Water Immersion	Shared Response	Sauna Bathing (Heat Exposure)
Autonomic Regulation	Sympathetic activation Catecholamine release Vasoconstriction	Heart rate variability ↑ Stress adaptation	Sympathetic activation Vasodilation Increased cardiac output
Vascular/Cardiovascular Adaptation	Brown adipose tissue activation	Endothelial function ↑ Nitric oxide ↑ Circulation ↑	Sweating/thermoregulation Heat shock protein expression
Cellular Stress Response	Mitochondrial biogenesis Autophagy induction	Heat shock proteins (HSPs) ↑ Anti-inflammatory signaling ↑ Tissue repair ↑	Anti-inflammatory effects
Metabolic Adaptation		Insulin sensitivity ↑ Lipid metabolism ↑ Energy expenditure ↑	

Note: HR indicates heart rate; HSPs, heat shock proteins.

Peptide Signaling (convergent downstream pathway): Hormonal signaling; anti-inflammatory effects; tissue repair/regeneration; metabolic regulation; angiogenesis.

Potential Outcomes in Women's Health: Cardiovascular health; metabolic health; mood & cognitive function; recovery & performance; hormonal balance & menopausal symptom relief; inflammation modulation.

2. Cold Water Immersion

Cold water immersion (CWI), typically defined as immersion in water at or below 15˚C (59˚F) for a minimum of 30 seconds and up to 15 minutes, induces a cascade of physiological responses beginning with the acute cold shock response [5]. The initial phase, lasting approximately 0 to 90 seconds, is dominated by sympathetic nervous system activation, characterized by rapid vasoconstriction, pronounced increases in heart rate and blood pressure, and a sharp elevation in circulating catecholamines—primarily norepinephrine. This sympathoadrenal surge is accompanied by involuntary gasping, hyperventilation, and increased peripheral resistance, mediated by alpha-adrenergic stimulation of cutaneous vessels. As immersion continues, the body transitions from acute sympathetic dominance toward progressive parasympathetic rebound, with baroreceptor feedback mechanisms moderating the cardiovascular response. With repeated CWI over weeks to months, this autonomic training effect manifests as measurable increases in resting heart rate variability (HRV), a marker of enhanced vagal tone that has been linked to improved stress resilience, anti-inflammatory signaling, and cardiovascular adaptability.

At the cellular level, repeated cold exposure initiates a hormetic adaptation process. Cold-shock proteins, including members of the RNA-binding protein family, are upregulated in response to thermal stress and contribute to enhanced cellular resilience, mitochondrial biogenesis, and anti-aging effects at the molecular level [6]. The transcriptional coactivator PGC-1α, a master regulator of mitochondrial biogenesis and oxidative metabolism, is activated through calcium/calmodulin-dependent kinase (CaMK) pathways stimulated by cold-induced muscle shivering and non-shivering thermogenesis, paralleling the mitochondrial adaptations seen with aerobic exercise training [7]. Brown adipose tissue (BAT) activation during cold immersion contributes to thermogenic energy expenditure and has garnered interest for its potential role in metabolic health, insulin sensitivity, and body composition. Notably, cold-induced thermogenesis in women during the follicular phase of the menstrual cycle has been informally reported to exceed that of men, which has been proposed as an estrogen-mediated enhancement of BAT responsiveness; this is an unpeer-reviewed observation from a secondary source [8] rather than an established finding, and it awaits confirmation in controlled trials with direct BAT measurement.

Clinical evidence supports CWI for reducing delayed onset muscle soreness (DOMS) and improving subjective recovery ratings following exercise in mixed-sex and predominantly male cohorts [9]. The female-specific evidence, however, is more equivocal than this general literature suggests: a 2025 randomized controlled trial enrolling women following exercise-induced muscle damage found that CWI produced no significant improvement in DOMS, muscle strength recovery, or creatine kinase relative to a passive control, and a related 2024 trial similarly found that cold (as opposed to hot) water immersion did not accelerate recovery of force-generating capacity in women [10] [11]. This discrepancy be-

tween the broader, largely male-derived CWI literature and the limited direct evidence in women underscores that post-exercise CWI benefits should not be assumed to generalize to female physiology without dedicated confirmation. However, timing relative to the type of training remains critical: immediate post-resistance training CWI attenuates mTOR and PGC-1α signaling pathways that drive hypertrophy and mitochondrial adaptation, blunting the anabolic response to strength training [12] [13]. For women seeking strength and hypertrophy gains, particularly perimenopausal women for whom lean mass preservation is a clinical priority, this timing consideration warrants particular attention.

Female-specific considerations for CWI extend across the menstrual cycle. During the follicular phase (days 1 - 14), rising estrogen is associated with greater stress resilience and may represent an optimal window for cold exposure, particularly for metabolic and performance purposes; this is an unpeer-reviewed practitioner observation [14] rather than a controlled finding. Evidence suggests that hormonal fluctuations during the menstrual cycle may influence autonomic responses to cold exposure. Some research has hypothesized that the follicular phase may be associated with greater tolerance to cold exposure. However, controlled laboratory studies directly comparing thermosensitivity across menstrual-cycle phases during cold water immersion have generally found no significant differences [15], so menstrual-phase-specific CWI recommendations are provisional pending further research. During the luteal phase (days 15 - 28), elevated progesterone raises basal body temperature and increases sensitivity to stressors, including cold; women report greater perceived difficulty with CWI during this phase, and the cortisol response may be more pronounced, with potential implications for progesterone production—an unpeer-reviewed practitioner observation [13] that has not yet been tested in controlled trials. For perimenopausal and postmenopausal women, cold immersion has been proposed as a strategy for vasomotor symptom management, on the hypothesis that thermoregulatory recalibration from repeated cold exposure could reduce the frequency and severity of hot flashes driven by estrogen withdrawal's effect on the hypothalamic thermostat. A large self-reported survey of regular cold-water swimmers found that a substantial subset of perimenopausal respondents reported improvement in hot flushes and other symptoms [16], but this observational, non-randomized design cannot establish causation, and no controlled trial has yet tested cold water immersion specifically for vasomotor symptoms; this application should therefore be considered preliminary. Contraindications to CWI include known or suspected cardiovascular disease, arrhythmias, Raynaud's disease, hypertension, and pregnancy, and immersion should never be undertaken alone or combined with alcohol or other central nervous system depressants.

3. Sauna Bathing

Sauna bathing produces systemic heat stress through passive whole-body exposure to temperatures typically ranging from 80˚C to 100˚C in traditional Finnish

dry saunas, resulting in a core body temperature elevation of 1˚C to 2˚C per session. This thermal load triggers a coordinated physiological response that closely parallels the hemodynamic effects of moderate-to-vigorous aerobic exercise: cardiac output increases by 50% - 70%, heart rate rises to 100 - 150 beats per minute, and peripheral vasodilation redistributes blood flow toward the skin surface to facilitate radiative heat dissipation [17]. Simultaneously, the heat stress activates heat shock proteins (HSPs)—particularly the HSP70 family—which function as molecular chaperones preventing protein aggregation, facilitating refolding of denatured proteins, and maintaining proteostasis that is progressively impaired during aging and cardiovascular disease [18]. Endothelial nitric oxide synthase (eNOS) is upregulated in the high-flow state of sauna bathing, increasing nitric oxide (NO) bioavailability, which plays a fundamental role in vascular tone regulation, prevention of atherosclerosis, and endothelial repair.

The cardiovascular evidence base for sauna bathing is the most robust among the three modalities reviewed. The landmark Finnish Kuopio Ischemic Heart Disease Risk Factor Study, which followed over 2,000 middle-aged participants for up to 20 years, established a striking dose-dependent relationship: individuals using a sauna four to seven times per week demonstrated a 63% reduction in sudden cardiac death, a 61% reduction in stroke risk, and significantly lower rates of hypertension compared to once-weekly users [19]. A 2026 systematic review and meta-analysis synthesizing evidence from large prospective cohort studies and randomized controlled trials confirmed these effects are mediated through upregulation of HSPs, modulation of the autonomic nervous system, and suppression of systemic inflammation, as reflected by reductions in C-reactive protein (CRP) and interleukin-6 (IL-6) [17]. Sauna use has also been associated with improvements in arterial stiffness, resting blood pressure, and lipid profiles across multiple trial designs [17]; it should be noted that a randomized crossover trial of infrared sauna in women did not find significant differences in arterial stiffness or blood pressure relative to exercise or rest, underscoring that these cardiovascular benefits are best supported for traditional Finnish sauna rather than infrared protocols [20].

A growing body of work has examined infrared sauna as an alternative to traditional Finnish sauna, operating at lower temperatures (approximately 45˚C to 60˚C) while producing comparable core temperature elevations through far-infrared wavelengths that penetrate more deeply into tissue. A randomized, controlled crossover trial conducted specifically in premenopausal women compared infrared sauna, aerobic exercise, and a rested control condition across measures of arterial stiffness, heart rate variability, and thermal response [20]. The study found that infrared sauna's physiological effects were driven primarily by thermoregulatory responses rather than direct exercise-mimetic cardiovascular activation, but still produced meaningful increases in core temperature and sympathovagal modulation. For women over 40, infrared sauna may be particularly accessible given its lower thermal intensity and suitability for those who cannot tol-

erate traditional high-heat environments, while still activating HSPs and anti-inflammatory pathways relevant to perimenopausal health.

For women in perimenopausal and postmenopausal stages, sauna therapy offers a specific cluster of benefits beyond general cardiovascular health. Vasomotor symptoms—hot flashes and night sweats—arise from estrogen withdrawal's disruption of the hypothalamic thermostat, rendering women abnormally sensitive to minor temperature fluctuations. Regular sauna use may recalibrate this thermoregulatory threshold through repeated deliberate heat exposure, reducing the frequency and severity of vasomotor episodes, and several small trials have demonstrated improvements in sleep quality and subjective well-being in this population [21]. The accelerated decline in skin collagen that occurs after menopause is also relevant: near-infrared wavelengths similar to those used in infrared saunas have shown capacity to stimulate fibroblast activity and collagen synthesis in photobiomodulation studies, potentially complementing the effects of collagen peptide supplementation [22]. Safety considerations for sauna use include adequate pre-session hydration, avoidance during febrile illness or active infection, and medical consultation for individuals with hypertension, cardiac arrhythmias, or conditions requiring strict thermal regulation. Table 2 summarizes the evidence hierarchy across all three modalities, ranking interventions by study design quality from randomized controlled trials down to preclinical and case-report-level evidence.

Table 2. Evidence hierarchy of thermal and peptide interventions in women's health.

Evidence Tier	Study Types	Example Interventions	Clinical Interpretation
Strong Evidence (High Quality)	Randomized controlled trials Meta-analyses Large prospective cohort studies	Sauna bathing (cardiovascular outcomes) GLP-1 receptor agonists Insulin therapy	Well-established clinical benefit
Moderate Evidence (Moderate Quality)	Smaller RCTs Controlled trials Prospective studies	Cold water immersion (recovery, soreness, mood) Sauna bathing (blood pressure, endothelial function) Certain therapeutic peptides	Promising evidence; further research needed
Limited Evidence (Low Quality)	Small studies Observational studies Mechanistic human studies	Contrast therapy Select peptides (e.g., growth hormone–releasing peptides, CJC-1295)	Preliminary/inconclusive evidence
Emerging/Preclinical Evidence (Very Low Quality)	Animal studies *In vitro* studies Case reports Expert opinion	BPC-157 TB-500 (Thymosin β-4 derivatives) Other experimental peptides	Investigational only; not established in humans

Note: Evidence quality generally decreases moving down the table (strong evidence reflects stronger clinical confidence; emerging/preclinical evidence carries greater uncertainty). RCT indicates randomized controlled trial; BP, blood pressure.

4. Peptides and Women's Health

Peptide therapy can be categorized into three evidence tiers. Tier 1 includes FDA-approved peptide therapeutics. Tier 2 includes predominantly off-label agents, for which human evidence exists but remains limited. Tier 3 includes investigational compounds such as BPC-157, MOTS-c, and humanin, whose proposed applications are supported primarily by preclinical studies and early-stage human research.

Peptides are short chains of amino acids that function as signaling molecules regulating metabolism, inflammation, and tissue repair [23]. Structurally, peptides occupy a strategic position between small molecules and biologics, offering high target specificity, favorable safety profiles, and a capacity to mimic endogenous ligands—particularly at G protein-coupled receptors (GPCRs) that regulate numerous physiological processes. Peptide-based therapeutics have grown from a niche research tool into a mainstream drug class, with dozens of FDA approvals achieved over the past decade and hundreds more candidates in clinical and preclinical development [24]. Despite this progress, the evidence base for many peptides in women's health remains heterogeneous, spanning rigorously validated pharmacologic agents to experimental compounds evaluated predominantly in animal models.

4.1. GLP-1 Receptor Agonists and Metabolic Health in Women (Tier 1: FDA-Approved)

Among the most clinically validated peptide therapies are glucagon-like peptide-1 (GLP-1) receptor agonists, including semaglutide and tirzepatide. These agents were originally developed to improve glycemic control in type 2 diabetes but have since demonstrated substantial benefits in weight management, cardiovascular risk reduction, and lipid regulation [25] [26]. Their relevance to women's health is particularly notable in the perimenopausal and postmenopausal periods, when declining estrogen promotes central adiposity, insulin resistance, and increased cardiometabolic risk. Preliminary data presented at the Endocrine Society's ENDO 2025 conference suggested that postmenopausal women using tirzepatide in combination with hormone therapy achieved greater weight reduction than those using tirzepatide alone, pointing to potential synergistic interactions between incretin-based therapy and estrogen replacement. For women who do not qualify for or choose not to use hormone therapy, GLP-1 receptor agonists represent a distinct but complementary strategy targeting the metabolic consequences of menopause rather than its vasomotor symptoms. The mechanism driving these benefits includes slowing gastric emptying, enhancing pancreatic insulin secretion, suppressing glucagon release, and modulating central appetite pathways in the hypothalamus [1].

4.2. Collagen Peptides and Musculoskeletal Support (Tier 1: Clinically Validated)

Hydrolyzed collagen peptides represent one of the most widely studied and com-

mercially accessible peptide categories for women. Collagen constitutes the primary structural protein in connective tissue, skin, tendons, and bone, and its synthesis declines progressively with age, a process accelerated by estrogen withdrawal following menopause [2]. Supplemental collagen peptides, delivered as hydrolyzed forms that are absorbed as di- and tripeptides, have shown capacity to stimulate fibroblast activity and upregulate endogenous collagen production [27]. Clinical trials have demonstrated improvements in skin elasticity, joint discomfort, and bone mineral density markers in postmenopausal women following regular collagen peptide supplementation. From a musculoskeletal perspective, collagen peptides have earned robust clinical validation—a distinction shared with GLP-1 receptor agonists but not with many other peptides currently being explored in regenerative medicine [28].

4.3. Growth Hormone Secretagogues and Body Composition (Tier 2: Off-Label, Limited Human Evidence)

Growth hormone secretagogue peptides, including sermorelin, ipamorelin, and CJC-1295, stimulate pituitary release of endogenous growth hormone (GH), which in turn promotes insulin-like growth factor-1 (IGF-1) production. These peptides are of particular interest in women experiencing age-related declines in GH secretion, which contribute to reductions in lean muscle mass, increases in adipose tissue, and diminished recovery capacity. Tesamorelin, a GH-releasing hormone analogue, holds FDA approval for HIV-associated lipodystrophy and represents a template for evidence-based secretagogue use. However, broader applications in women's anti-aging or body composition protocols remain off-label and lack large-scale randomized controlled trial data. Clinicians considering these agents for perimenopausal or postmenopausal patients must weigh theoretically plausible benefits in muscle preservation against unknowns related to long-term safety, particularly given the mitogenic potential of sustained GH and IGF-1 elevation [29].

4.4. BPC-157 and Tissue Regeneration (Tier 3: Investigational)

Body Protection Compound-157 (BPC-157) is a synthetic 15-amino acid pentadecapeptide originally isolated from human gastric juice and characterized by broad cytoprotective and regenerative properties across multiple tissue systems. Mechanistically, BPC-157 promotes angiogenesis by upregulating vascular endothelial growth factor (VEGF), stimulates fibroblast proliferation and collagen synthesis through focal adhesion kinase (FAK)-paxillin signaling, and increases growth hormone receptor (GHR) expression in fibroblasts—collectively accelerating tissue repair in tendons, ligaments, skeletal muscle, and the gastrointestinal mucosa [30]. Preclinical rodent studies summarized in that review have demonstrated significantly improved biomechanical strength and collagen organization in repaired tendons, enhanced satellite cell activity and muscle fiber regeneration following injury, and chondroprotective effects relevant to osteoarthritis. A small

retrospective study by Lee and Padgett [31] reported meaningful pain reduction in 87.5% of patients receiving intra-articular knee injections containing BPC-157, and a 2024 pilot study by Lee and colleagues [32] documented high rates of resolution in interstitial cystitis following intravesicular administration, with no reported adverse effects in either cohort. These findings are preliminary and must be interpreted cautiously given small sample sizes and the absence of controlled trial designs. Importantly, BPC-157 remains without FDA approval for human therapeutic use, and its classification as an investigational compound means that compounded or commercially sourced preparations carry risks related to purity, dosing accuracy, and regulatory compliance [33]. For women, the compound's potential relevance spans recovery from exercise-related musculoskeletal injury, gastrointestinal support during concurrent GLP-1 therapy, and possible neuroprotective effects via modulation of dopaminergic and serotonergic pathways—though none of these applications has been confirmed in human clinical trials.

4.5. Mitochondrial and Longevity-Oriented Peptides (Tier 3: Investigational)

An emerging category of peptides targets mitochondrial function and cellular aging pathways, with compounds such as humanin, MOTS-c, and elamipretide generating increasing scientific interest. MOTS-c, encoded within mitochondrial DNA, has demonstrated roles in regulating skeletal muscle metabolism, insulin sensitivity, and exercise-responsive adaptations in preclinical models [34]. These mitochondrially derived peptides are particularly relevant to women's health given the convergence of hormonal decline and mitochondrial dysfunction that characterizes the perimenopausal transition. Elamipretide has shown promise in models of cardiovascular aging and heart failure by stabilizing the inner mitochondrial membrane. Clinical translation of this compound class remains at an early stage, with most evidence still confined to preclinical and early-phase human research. The field is moving toward biomarker-guided, personalized protocols that pair specific peptides to individual hormonal profiles, metabolic signatures, and recovery goals—an approach with particular implications for women navigating the physiological complexity of midlife transition.

Regulatory Considerations and Clinical Oversight. The landscape of peptide therapeutics is characterized by significant regulatory heterogeneity. GLP-1 receptor agonists such as semaglutide and tirzepatide have undergone rigorous FDA evaluation and hold approval for specific indications including type 2 diabetes and chronic weight management. In contrast, many peptides widely promoted in wellness and integrative medicine settings—including BPC-157, TB-500, and certain growth hormone secretagogues—occupy a grey area of regulatory status, often marketed as "research compounds" and unavailable for legal prescription outside clinical trials. The FDA's expansion of Import Alert 66 - 78 to include additional unapproved peptides, combined with tightened DEA oversight of certain growth hormone secretagogues, signals increasing regulatory scrutiny [33]. Quality con-

trol concerns compound this challenge: independent testing has found that a substantial proportion of commercially available compounded peptides contain incorrect dosages or undeclared ingredients [33]. For clinicians working with women seeking peptide-based interventions, these considerations demand a framework that distinguishes rigorously validated pharmacologic agents from experimental compounds, ensures sourcing from FDA-registered 503B outsourcing facilities when compounding is involved, and applies informed consent processes that transparently address the current state of evidence and regulatory risk. Table 3 consolidates practical protocol guidance—temperature, duration, frequency, and key clinical considerations—for cold water immersion, sauna bathing, and contrast therapy to support this kind of individualized, risk-aware counseling.

Table 3. Protocol guidelines for clinical application.

	Cold Water Immersion	Sauna Bathing (Heat Therapy)	Contrast Therapy (Heat + Cold Alternation)
Temperature	10 - 15˚C (50 - 59˚F)	75 - 100˚C (167–212˚F)	Heat: 38 - 42˚C (100 - 108˚F) Cold: 10 - 15˚C (50 - 59˚F)
Duration	2 - 10 minutes	10 - 20 minutes	3 - 5 cycles (Heat: 3 - 4 min/Cold: 1 - 2 min)
Frequency	2 - 5 times per week	3 - 7 times per week	2 - 4 times per week
Primary Goals	Reduce inflammation & soreness Enhance recovery Improve mood & alertness	Cardiovascular health Blood pressure regulation Menopausal symptom relief Stress reduction	Improve circulation Reduce muscle soreness Enhance autonomic flexibility
Key Considerations	Avoid immediately after resistance training if hypertrophy is the goal Avoid in Raynaud's phenomenon, severe cardiovascular disease	Hydrate before and after Not recommended in uncontrolled hypertension or severe heart disease Stop if dizziness or discomfort occurs	Ensure adequate hydration Not recommended in uncontrolled hypertension or severe heart disease Discontinue if lightheaded

Note: Protocols derived from current literature and expert consensus; adjust based on individual tolerance and clinical judgment.

General Notes

Individualize protocols based on health status, tolerance, and goals.

Monitor for adverse symptoms (dizziness, nausea, chest pain, excessive fatigue).

Combine with healthy lifestyle habits (nutrition, exercise, sleep) for optimal benefits.

Populations Requiring Medical Clearance: Pregnancy, uncontrolled hypertension, severe cardiovascular disease, heat/cold intolerance, active infection, neurological disorders.

5. Discussion

Thermal therapies and peptide signaling converge on a set of shared physiological

pathways that constitute a unifying mechanistic framework for their collective relevance to women's health. Chief among these convergent pathways are autonomic nervous system modulation, mitochondrial adaptation, vascular remodeling, and cellular stress signaling. Cold water immersion and sauna bathing, despite producing opposing thermal stimuli, both activate robust neuroendocrine responses that recalibrate autonomic balance: CWI through an initial sympathetic surge followed by parasympathetic rebound and increased HRV, and sauna bathing through heat-induced vasodilation and biphasic autonomic modulation involving both sympathetic activation during heat exposure and parasympathetic recovery afterward [17]. This shared autonomic recalibration is clinically significant in women, given that reduced HRV and impaired autonomic regulation are independent predictors of cardiovascular risk that worsen with the hormonal shifts of menopause. Peptide therapies intersect this framework through their roles in vascular regulation, metabolic signaling, and cellular repair—GLP-1 receptor agonists, for instance, exert direct cardioprotective and autonomic-modulating effects beyond their glycemic actions [26].

A critical pattern emerges when the evidence base is examined rather than simply re-tabulated (see **Table 2** and the preceding sections for tier-by-tier detail): the interventions with the strongest mechanistic rationale for female-specific application—menstrual-phase-dependent CWI responses, thermally mediated vasomotor symptom relief—are precisely those with the thinnest direct evidentiary support, while the modalities with the deepest overall evidence base, such as sauna cardiovascular outcomes and GLP-1 metabolic effects, were established largely in cohorts and endpoints not designed to test female-specific mechanisms. This inversion, rather than a simple ranking of which modality is \"most effective,\" is the central epistemic problem this review surfaces. It implies that clinical guidance should weight not only the overall evidence tier of a therapy, but whether the specific claim being extended to a female patient has itself been tested in women.

A critical limitation of this review, and of the broader field, is the persistent gap in female-specific data. The majority of seminal studies on thermal therapies were conducted in male-dominant or male-only cohorts, and even when women were included, analyses were rarely stratified by menstrual phase, menopausal status, or hormonal context—variables that materially alter physiological responses to thermal stress [3]. Similarly, peptide therapy research has been conducted predominantly in male animal models and male human participants, leaving the female hormonal and metabolic context largely unexplored. This is particularly consequential given the growing recognition that women are not simply smaller men physiologically: sex hormones modulate receptor expression, autonomic tone, thermoregulatory thresholds, adipose tissue biology, and inflammatory signaling in ways that can fundamentally alter both the magnitude and the nature of responses to these interventions.

From a clinical integration standpoint, these three modalities are not mutually

exclusive and may produce additive or synergistic benefits when combined thoughtfully. The Nordic practice of alternating sauna and cold water immersion—often referred to as contrast therapy—is proposed to leverage the opposing vascular responses of heat-induced vasodilation and cold-induced vasoconstriction to produce a pumping effect on peripheral circulation and, potentially, a more pronounced autonomic training signal than either modality alone; as noted above, this remains a theoretical extrapolation pending controlled comparative trials, particularly in women. Peptide therapies, particularly collagen peptides and GLP-1 receptor agonists, may complement thermal modalities by supporting the musculoskeletal and metabolic substrates upon which the benefits of thermal stress depend. Emerging clinical frameworks in regenerative and integrative medicine are beginning to formalize these combinations into protocol-based approaches tailored to individual hormonal profiles, fitness levels, and health goals—a personalized medicine paradigm that aligns well with the heterogeneous physiological landscape of women's health across the lifespan.

6. Conclusions

Cold water immersion, sauna bathing, and peptide-based interventions converge on a shared set of physiological pathways—autonomic modulation, vascular remodeling, and mitochondrial adaptation—that position them as a coherent, systems-based framework for women's health rather than three unrelated modalities. Sauna bathing offers the deepest cardiovascular evidence base of the three; cold water immersion and peptide therapies span a wider range from well-validated (GLP-1 agonists, collagen peptides) to investigational (BPC-157, mitochondrial peptides), with the comparative strength of evidence for each detailed in **Table 2** and the corresponding sections above.

The central limitation across this field is the persistent underrepresentation of women—and especially women stratified by hormonal context—in clinical research. Addressing this gap is not merely a matter of equity; it is a scientific necessity, given that female physiology meaningfully alters thermoregulatory, autonomic, and metabolic responses to these interventions. Future research priorities should include randomized controlled trials of CWI and sauna bathing in female-only cohorts stratified by menstrual phase and menopausal status; mechanistic studies examining how estrogen and progesterone modulate responses to thermal stress; dose-finding trials for emerging peptide therapies in female populations with relevant comorbidities; and investigations of combined thermal-peptide protocols that leverage their convergent pathways. Standardization of intervention protocols—temperature, duration, frequency, and timing relative to the menstrual cycle—is essential to enable cross-study comparison and the development of evidence-based clinical guidelines. As the evidence base matures, these modalities hold substantial promise for a personalized, integrative approach to women's health that honors the complexity of female physiology rather than treating it as a variation from a male default.

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Conceptualization, N.C.; methodology, N.C. and L.N.; investigation, N.C., L.N., L.G., and R.B.; writing—original draft preparation, N.C.; writing—review and editing, N.C., L.N., L.G., and R.B.; supervision, R.B. All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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