

Clinical Effects of Regular Dry Sauna Bathing: A Systematic Review

Dr Joy Hussain and Professor Marc Cohen

School of Health and Biomedical Sciences, RMIT University, Australia

Abstract

Introduction Many health benefits are claimed by individuals and facilities promoting sauna bathing, however the medical evidence to support these claims is not well established. This paper aims to systematically review recent research on the effects of repeated dry sauna interventions on human health. *Methods* A systematic search was made of medical databases for studies reporting on the health effects of regular dry sauna bathing on humans from 2000 onwards. Risk of bias was assessed according to the Cochrane Collaboration guidelines. *Results* Forty clinical studies involving a total of 3855 participants met the inclusion criteria. Only 13 studies were randomized controlled trials and most studies were small ($n < 40$). Reported outcome measures were heterogeneous with most studies reporting beneficial health effects. Only one small study ($n = 10$) reported an adverse health outcome of disrupted male spermatogenesis, demonstrated to be reversible when ceasing sauna activity. *Conclusions* Regular dry sauna bathing has potential health benefits. More data of higher quality is needed on the frequency and extent of adverse side effects. Further study is also needed to determine the optimal frequency and duration of distinct types of sauna bathing for targeted health effects and the specific clinical populations who are most likely to benefit.

Keywords

Finnish Sauna, Infrared Sauna, Whole body thermotherapy, Hormesis

Introduction

Sauna bathing is a form of whole body thermotherapy that has been used in various forms (radiant heat, sweat lodges, etc.) for thousands of years in many parts of the world for hygiene, health, social and spiritual purposes. Modern day sauna use includes traditional Finnish-style sauna, along with Turkish-style Hammam, Russian Banya and other cultural variations, which can be distinguished by the style of construction, source of heating and level of humidity. Traditional Finnish saunas are the most studied to date and generally involve short exposures (5 -20 minutes) at temperatures of 80°C – 100°C with dry air (relative humidity of 10% to 20%) interspersed with periods of increased humidity created by the throwing of water over heated rocks.[1] In the past decade, infrared sauna cabins have become increasingly popular. These saunas use infrared emitters at different wavelengths without water or additional humidity and generally run at lower temperatures (45 – 60°C) than Finnish saunas with similar exposure times. [2] Both traditional Finnish and infrared sauna bathing can involve rituals of cooling-off periods and rehydration with oral fluids before, during and/or after sauna bathing.

Sauna bathing is inexpensive and widely accessible with Finnish-style saunas more often used in family, group and public settings and infrared saunas more commonly built and marketed for individual use. Public sauna facilities can be located within exercise facilities and the relationship between saunas and exercise, which may include synergistic hormetic responses, is an area of active research.[3-8] The use of private saunas especially involving infrared saunas, is also increasing and saunas are used for physical therapy in massage clinics, health spas, beauty salons and domestic homes. This trend is capitalising on the call for additional lifestyle interventions to enhance health and wellness particularly in populations that have difficulty exercising (e.g. obesity, chronic heart failure, chronic renal failure, chronic liver disease).[9] Facilities offering sauna bathing often claim health benefits that include detoxification, increased metabolism, weight loss, increased blood circulation, pain reduction, anti-aging, skin rejuvenation, improved cardiovascular function, improved immune function, improved sleep, stress management and relaxation. However, rigorous medical evidence to support these claims is scant and incomplete, as emphasized in a recent multidisciplinary review of sauna studies.[10]

There is considerable evidence to suggest that sauna bathing can induce profound physiological effects.[4, 11-17] Intense short-term heat exposure elevates skin temperature and core body temperature and activates thermoregulatory pathways via the hypothalamus [18] and CNS (central nervous system) leading to activation of the autonomic nervous system. The activation of the sympathetic nervous system, hypothalamus-pituitary-adrenal hormonal axis and the renin-angiotensin-aldosterone system leads to well-documented cardiovascular effects with increased heart rate, skin blood flow, cardiac output and sweating.[1, 11] The resultant sweat evaporates from the skin surface and produces cooling that facilitates temperature homeostasis. In essence, sauna therapy capitalises on the thermoregulatory trait of homeothermy, the physiological capability of mammals and birds to maintain a relatively constant core body temperature with minimal deviation from a set point.[19] It is currently unclear whether steam saunas invoke the same degree of physiological responses as dry saunas[20], as the higher humidity results in water condensation on the skin and reduced evaporation of sweat. [21]

On a cellular level, acute whole-body thermotherapy (both wet and dry forms) induces discrete metabolic changes that include production of heat shock proteins, reduction of reactive oxygenated species, reduced oxidative stress and inflammation pathway activities, increased NO (nitric oxide) bioavailability, increased insulin sensitivity and alterations in various endothelial-dependent vasodilatation metabolic pathways.[22] It has been suggested that heat stress induces adaptive hormesis mechanisms similar to exercise, and there are reports of cellular effects induced by whole body hyperthermia in conjunction with oncology-related interventions (i.e. chemotherapy and radiotherapy)[23]; however the mechanisms by which the physiological and cellular changes induced by sauna bathing contribute to enhanced health and/or therapeutic effects is still being explored.[4, 7, 8, 24-27]

The following systematic review was undertaken to explore recent research on the clinical effects of repeated dry sauna bathing (Finnish-style, infrared or other dry sauna forms) to document the full range of medical conditions saunas have been used for, as well as any associated health benefits and/or adverse effects observed. While a small number of reviews of sauna bathing and health have been conducted in the past[1, 2, 28-30], as far as we know, this is the first systematic review of sauna and health to include both Finnish and infrared saunas. Furthermore, this review only considers effects related to regular, multiple sessions of sauna activity rather than single sauna sessions, to better reflect the use of sauna bathing use as a regular lifestyle intervention.

Methods

PRISMA guidelines for conducting systematic reviews were followed, including the use of validated tools to assess the risk of bias in randomised controlled trials. [31-33]

Eligibility criteria

Studies of humans undergoing repeated dry sauna bathing that reported on health measures were included in the review. Studies were included for initial review if they were published in English language from January 2000 onwards and involved research in humans undergoing repeated dry sauna sessions with at least one reported health outcome. Studies involving predominantly high-humidity (>50%) wet/steam 'sauna' or immersion hydrotherapy were excluded for the potential confounding mechanisms of differential sweating rates and explicit focus of this review limited to 'dry sauna' interventions. Studies of partial body heating were excluded since proposed mechanisms of action may or may not be the same as whole body heating. Studies reporting primarily animal-based, non-human findings were excluded given the recognized differences in end-organ (skin) structure and responses (sweating mechanisms) between animals and humans. Studies of 'sauna' as a recruitment venue for potential sexual activity, primarily regarding men who have sex with men (MSM), were excluded since these studies lacked details of sauna interventions, confounding whether wet or dry interventions, and measured health metrics focused to sexual activity but not necessarily to sauna activity.

Search Strategy

PubMed, Web of Science, Scopus, and Proquest were initially searched with keyword "sauna" and date restrictions of January 2000 – April 2017. Search dates were chosen to focus on updated findings reflecting advancing technology in both diagnostics and physiological monitoring to build upon the foundational literature of prior non-systematic clinical reviews of sauna activity published in the early 2000s. After further restrictions of English language and humans, records were then expanded using Google Scholar, with searches for other research by key authors, searches of citations and reference lists of original and review articles, and other "related articles". Additional searches with expanded keywords relating to sauna including "interventional study", "whole body hyperthermia" and "whole body thermotherapy" were also conducted with the same initial restrictions.

Data Extraction

Abstracts of initially identified studies were screened by investigator JH and then the complete full-text articles of potentially eligible studies were carefully screened by both investigators JH and MC for research design, population descriptive data, timing and physical details of dry sauna intervention, outcome measures, key results, and adverse effects. Discrepancies regarding inclusion of studies or data extraction were discussed until consensus reached.

Assessment for risk of bias

Included randomised controlled trials (RCTs) were assessed for risk of bias according to the Cochrane collaboration's tool for assessing bias and calculated JADAD scores[33]. Domains of bias assessed were selection bias (by looking for random sequence generation and allocation concealment), performance bias (by published mention of blinding of participants and personnel), detection bias (by documented attempts to blind outcome assessment), attrition bias (by evaluating for incomplete outcome data), reporting bias (by any indication of selective reporting of outcomes) and other bias (e.g. conclusions not clearly supported by reported outcomes). Risk of bias was initially assessed by investigator JH as 'low', 'unclear' or 'high', then confirmed by investigator MC. Any discrepancies were discussed until consensus reached.

Figure 1 – PRISMA flow diagram of evidence searches and inclusions/ exclusions.

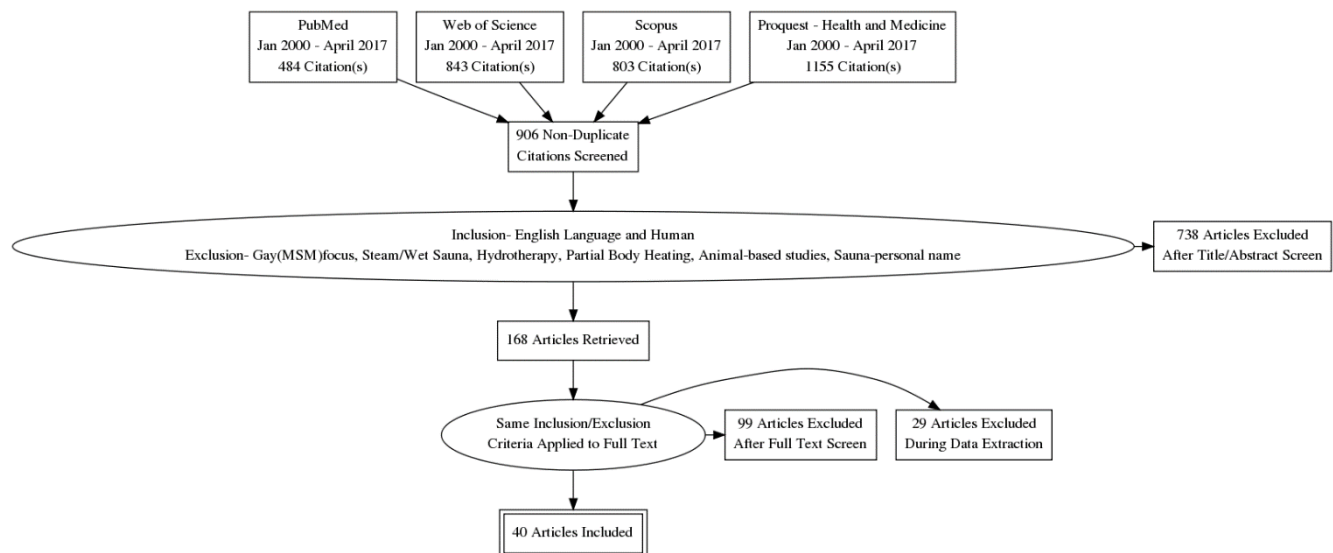


Figure 2 - Levels of Evidence

Level I: Multi-centre or single-centre, randomized controlled trial (RCT)

Level II: Controlled interventional trial; prospective cohort study

Level III: Retrospective comparative study; case-control study; pilot study

Figure 3 – Risk of bias assessment in Randomized Controlled Trials

Fujita 2011	✗	?	✗	✗	✓	✓	?	<3
Huppe 2009	✗	?	✓	✓	✓	✗	?	<3
Kanji 2015	✓	✓	✓	✓	✓	✓	✓	4
Kihara 2004	✗	?	✗	✗	✓	?	?	<3
Kunbootsri 2013	✗	?	✗	✗	✓	✓	?	<3
Kuwahata 2011	✗	?	✗	✗	✓	✓	?	<3
Masuda 2004	✗	?	✗	✗	✓	✓	✗	<3
Masuda 2005 -pain	✓	?	✗	✗	✓	✓	✗	<3
Masuda 2005 - depression	✗	?	✗	✗	✓	✓	✗	<3
Miyata 2008	✗	?	✗	✗	✓	✓	?	<3
Pach 2010	✓	?	✓	✓	✓	✓	?	5
Shinsato 2010	✗	?	✗	✗	✓	✓	?	<3

Tei 2016	✓	?	✗	✓	✓	✓	?	3
	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias	JADAD score[33]

✓ Low risk of bias ✗ High risk of bias ? Unclear risk of bias

Results

Literature Search

Figure 1 summarises the screening and assessment strategies used with the search results. Of the 906 non-duplicate citations initially identified, 738 were excluded after a review of the abstracts.

After retrieving 168 full-text articles and applying the same exclusion criteria as discussed above along with excluding review articles, case reports, and letters to the editor, 69 independent human studies involving dry sauna interventions were identified for further analysis.

In the data extraction step, one study was excluded since it was essentially a case series with two patients, mistakenly identified as an interventional trial conducted by a key author. [34] Another 28 studies were excluded due to the intervention being only a single session of sauna and not repeated sauna therapy, which is the stated focus of this review.

A total of 40 studies remained for inclusion in this systematic review. A summary of extracted data is presented in Tables 1 – 7, with tables categorised according to participant population.

Study Design

Of the forty studies, 13 were randomised controlled trials (RCTs), 6 were trials with un-randomised control groups and 2 were prospective cohort studies. The remainder of studies were single- or multi-group interventional trials (without a control group) or retrospective studies. Figure 2 presents three levels of evidence used to help stratify the quality of the studies.

Limitations/ Risk of Bias

Many studies were relatively small, with limited number of participants and limited numbers of randomized studies were available for review. Of the 13 randomized controlled trials (RCTs) identified, only 3 of these studies (involving 343/840 participants)[35-37] were assessed with having a low overall risk of bias according to the Cochrane Collaboration criteria[32] and a Jadad score >3 [33]. Nine of these 13 RCTs enrolled fewer than 50 participants. Figure 3 summarises the assessments of the RCTs for overall risk of several types of bias.

The follow-up time of many of the studies was relatively short, in the order of weeks to months, thereby possibly compromising detectability and reporting of long-term health effects over years.

Setting and Participant Characteristics

The reviewed studies included a total of 3855 participants living in 12 different countries. Over half of the studies (22 of 40) originated in Japan. The smallest study involved Australian athletes (n=7) and the two largest studies (both prospective cohort studies) involved the same cohort of 2315 Finnish men[38-40]. Most studies had small sample sizes with over half (21 of 40 studies) involving 30 or less participants.

The studies involved a range of healthy and disease populations with 6 studies of healthy individuals, 19 studies of people diagnosed with cardiovascular disease (CVD) or increased risk for CVD (i.e. congestive heart failure, type 1 or

type 2 diabetes mellitus, peripheral arterial disease), 7 studies of patients diagnosed with rheumatological, chronic pain or mood disorders, 4 studies of patients diagnosed with airway-related disorders (i.e. Chronic obstructive pulmonary disease, Allergic rhinitis), 2 studies of elite athletes, and 2 studies of populations overburdened with environmental toxicants.

Interventions

Eleven studies investigated the use of Finnish saunas and 25 studies utilised infrared sauna interventions. The remainder 4 studies used other forms of dry sauna (Thai-style or mixed). Sauna sessions varied from 5 minutes to 20 minutes in single or multiple sessions totalling 30 minutes – 4 hours daily, once to several times each week over study durations that ranged from 3 days to 5 months. The cohort studies followed frequent infrared sauna bathers for 5 years and frequent male Finnish sauna bathers for over 20 years.

All of the studies involving Finnish-style saunas used interventions ranging in temperature from 80 – 90°C with relative humidity levels of 10 – 20% except Huppe-2009, a study comparing detoxification protocols, which employed a lower temperature sauna at 50 – 65°C with 30% relative humidity for 15 minutes in one intervention arm. [41]

Of the 25 studies involving infrared sauna, all used far-infrared types except Ross-2012, which employed a full spectrum infrared sauna as part of a detoxification protocol for policemen[42]. All infrared sauna studies entailed sauna exposures at 60°C for 15 – 30 minutes with the exception of two studies: Amano-2015 studying the effects of sauna on patients diagnosed with chronic fatigue syndrome/ myalgic encephalomyelitis (CFS/ME) using saunas set at 40°C – 45°C for 15 minute sessions [43]; and Oosterveld-2009 examining the effects of sauna set at 55°C for 30 minute sessions on patients diagnosed with Ankylosing Spondylitis and Rheumatoid Arthritis.[44]

All of the sauna interventions were conducted in supervised settings (i.e. in-hospital, rehabilitation hospitals, health centres, university or medical laboratories, outpatient programs) except Kanji-2015, which provided sauna voucher cards to allow participants to attend saunas of choice attached to local swimming pools[36] and the two large cohort studies that followed Finnish men attending saunas of their choice[38, 39].

Outcome Measures

Some studies focused solely on measuring subjective quality of life and symptom scoring surrounding sauna activity such as SF-36 (36-item short form health survey), FASE (Foundation for Advancements in Science and Education) 50-item survey of symptoms and sleep, CMI (Cornell Medical Index) survey of somatic complaints; VAS (visual analogue scales) for hunger, relaxation, specific types of pain (i.e. leg pain); various numeric rating scales for pain, fatigue, sleep quality, and common cold symptoms; validated tools for depression, anxiety, headache disability, and anger such as POMS (profile of mood states) questionnaire, BDI (Beck Depression Inventory), SRQ-D (self-rating questionnaire for depression), Zung SDS (self-rating depression scale), STAI (state-trait anxiety inventory questionnaire) and HDI (Headache Disability Index).[36, 42, 43, 45-47]

Other interventional studies focused on obtaining objective measures related to sauna activity. For example, the studies involving CHF patients tracked combinations of physiological changes using body weight, body temperature, HR (heart rate) or PR (pulse rate), SBP and DBP (systolic and diastolic blood pressures); exercise tolerance using the 6MWD (6-minute walking distance) and peak VO₂ (peak/maximum volume of oxygen) on bicycle ergometer; cardiomegaly/ heart enlargement using CTR (cardiothoracic ratio) on CXR (chest X-ray); cardiac flow performance using standard ECHO (echocardiogram) doppler ultrasound parameters; overall functional state using clinician-based NYHA (New York Heart Association) classification; endovascular reactivity using FMD (flow-mediated dilation of brachial artery); heart failure activity using plasma levels of BNP (B-natriuretic peptide); autonomic nervous system and immune-mediated activity using ECG (electrocardiogram) recordings with heart rate variability parameters and plasma levels of norepinephrine, TNF- α (tumour necrosis factor – alpha) and CD34+ (cluster of differentiation 34, bone marrow derived) cells; endovascular activity using plasma levels of VEGF (vascular endothelial growth factor), nitric oxide metabolites (nitrate and nitrite), and reactive oxygen metabolites (hydroperoxide).[35, 48-55] Studies involving patients with increased cardiovascular risk or studies of healthy patients with aims to detect changes in cardiovascular risk with sauna activity used some of the same physiological parameters mentioned above as well as serum lipid profiles (total cholesterol, LDL, HDL and triglycerides), fasting plasma glucose levels, serum levels of uric

acid (potential marker of insulin resistance and metabolic syndrome), plasma levels of ghrelin, serum levels of leptin, plasma levels of Hb (haemoglobin) and HCT (haematocrit), and urinary prostaglandin levels.[56-61]

Other specific objective outcome measures performed before/after sauna include: myocardial perfusion scintigraphy with adenosine, treadmill exercise stress test results, flow-mediated vasodilation of brachial artery and expression of CD34-positive bone marrow-derived cells in hospital patients with ischaemic heart disease and total coronary occlusion; standard spirometry parameters, peak nasal inspiratory flows, and ECG (electrocardiogram) with HRV (heart rate variability) parameters in participants diagnosed with allergic rhinitis; plasma volume changes (calculated from hemoglobin readings), hydration status using urine specific gravity, exercise performance on ergometer, and ECG with HRV parameters in elite athletes; axillary body temperatures, venous blood gas panels, lipid peroxidation by UV (ultraviolet light) and fluorescence analysis, and nitric oxide levels in elite athletes; trans-epidermal water loss, stratum corneum hydration, skin erythema, skin surface pH, surface sebum contents, and NaCl (sodium chloride) concentrations in sweat of healthy men and women; basic physiological observations (temperature, heart rate, blood pressure, body weight), calculated plasma volumes, and serum levels of thyroid function (TSH – thyroid stimulating hormone, T3, T4) and other hormones (human growth hormone, ACTH - Adrenocorticotropic hormone, and cortisol) in healthy women; and pre-and post-intervention semen analysis including standard sperm parameters, sperm chromatin structure analysis, sperm apoptosis, quantitative sperm heat stress gene expression levels, and plasma levels of male sex hormone levels (LH – luteinizing hormone, FSH – follicle stimulating hormone, testosterone, inhibin) in healthy men.

Other interventional studies employed a combination of subjective and objective measures. Shinsato-2010 and Tei-2007 compared VAS for leg pain as well as 6MWD (6-minute walking distance), ABI (ankle/brachial index), leg blood flows with doppler laser imaging and angiography, gene expression levels of CD34+ blood cells and serum levels of VEGF, nitrates and nitrites in patients hospitalised with peripheral artery disease.[62, 63] Kikuchi-2014 and Umehara-2008 assessed modified Borg dyspnoea scale or SGRQ (St George's Respiratory Questionnaire) in addition to basic physiological observations (temperature, BP, HR, respiratory rate, O₂ saturation), standard spirometry and ECHO parameters, 6MWD or ergometer exercise tolerance, and plasma levels of BNP, HCT and albumin in hospitalised patients with COPD.[64, 65] Oosterveld-2009 utilised subjective VAS and validated tools of EPM-ROM (Escola Paulista de Medicina- range of motion), DUTCH-AIMS (Dutch arthritis impact measurement scales), BASMI (Bath Ankylosing Spondylitis functional index range of motion), and BASDAI (Bath Ankylosing Spondylitis disease activity index), as well as serum levels of ESR (erythrocyte sedimentation rate).[44] Huppe-2009 used several self-assessed validated scoring tools: Beschwerden-Liste 24-item questionnaire of somatic symptoms, ADS-L/CES-D 20-item questionnaire of general depression, SF-36 quality of life questionnaire. Objective tests of neuropsychological processing speed (GT-MT/ZVT scoring), concentration (attention test d2), memory power and speed (WL-N and WL-G scoring, respectively), as well as serum levels of three different PCB (polychlorinated biphenyl) congeners, hexachlorobenzene, DDT (dichlorodiphenyltrichloroethane), and DDE (p-dichlorodiphenylethylene) were measured before and/or after sauna interventions.[41]

The two largest prospective cohort studies (n=2315) tracked the incidence of dementia, Alzheimer's disease and other cardiovascular disease-related outcomes such as sudden cardiac death, fatal coronary artery disease, fatal cardiovascular disease and all-cause mortality over 20+ years, stratified by sauna bathing one time each week, 2 -3 times each week, or 4 -7 times each week.[38, 39] The one retrospective cohort study (n = 129) tracked episodes of cardiac death, cardiac events, and re-hospitalisations due to congestive heart failure after completion of an in-hospital 5-day sauna program followed by twice weekly outpatient sauna activity over 5 years.[66]

Health Outcomes

Cardiovascular Disease

The findings of the 9 studies that researched sauna therapy for congestive heart failure (CHF) in adults culminated in the largest and most recent prospective multi-centred randomised controlled trial involving 149 patients with advanced CHF that demonstrated small but improved 6-minute walking distances (-44.9m +/- SD 49.3 m, p<0.05), reduced cardio-thoracic ratios on chest X-ray (-1.58% +/- SD 2.81%, p< 0.05) reflecting reduced heart sizes and improved NYHA (New York Heart Association) classifications of disease (fewer class III and IV patients, p<0.05) after 2 weeks of sauna therapy, all compared to no significant respective changes in a control group that received standard medical care.[35]

A study of 12 infants with ventricular septal defects (VSDs) and related severe CHF (congestive heart failure) who underwent sauna bathing for 5 minutes daily for 4 weeks demonstrated decreased VSD (ventricular septal defect) shunt flow ratios ($p < .05$), which averted the need for surgical repair in 9 infants.[54]

Another randomised controlled trial examined the effects of repeated sauna therapy on ventricular arrhythmias in 30 subjects with congestive heart failure and more than 200 premature ventricular contractions (PVCs) per 24 hours at baseline and reported significantly fewer PVCs (mean 848 +/- 415 vs baseline mean 3097 +/- 1033 per 24 hours, $p < 0.01$) after 2 weeks of repeated sauna sessions compared with no significant changes in a control group that received conventional medical therapy.[53]

Two studies investigated the effects of repeated sauna sessions on patients with peripheral arterial disease. The first study was a pilot trial which reported decreased visual analogue scale (VAS) pain scores ($p < 0.01$), improved 6-minute walking distance (6MWD) ($p < 0.01$), improved ankle/brachial index (ABI) ($p < 0.01$), and an increase in visible collateral vessels in ischaemic legs with digital subtraction angiography ($p < 0.01$) observed after 10 weeks of repeated sauna therapy in twenty patients.[63] The second study was a randomised controlled trial ($n = 21$) which reported similar decreases in VAS (visual analogue scale) leg pain scores ($p < 0.05$), increases in 6MWD ($p < 0.01$) and improved ABI ($p < 0.01$) in the sauna treatment group compared with no change in the control group that received conventional medical therapy. The investigators of this second study also demonstrated a 2-fold increase in mRNA CD34/GAPDH expression in peripheral blood mononuclear cells ($p = .015$) and increases in serum nitrate and nitrite levels ($p < .05$, $p < .05$) in the sauna group with no respective changes in the control group and no significant changes in serum VEGF levels in either group .[62]

Another randomised controlled trial examined the effects of repeated sauna therapy on 24 ischaemic heart disease subjects with chronic total occlusion of coronary arteries detected on coronary angiogram who had failed or rejected attempts at percutaneous coronary intervention or who had vessels deemed unsuitable for operative interventions. This study revealed that after 3 weeks of daily (5 times weekly) infrared sessions, the scoring indices of defect reversibility on myocardial perfusion scans (summed stress scores and summed difference scores) improved (16 +/- 7 to 9 +/- 6, $p < 0.01$ and 7 +/- 4 to 3 +/- 2, $p < 0.01$) after sauna therapy but not in the control group that received standard medical care.[67]

The two largest studies of this review, which prospectively followed 2315 men in Finland over 20.7 years of frequent sauna bathing for cardiovascular disease-related outcomes used multivariate analysis and calculated hazard ratios (HR) adjusting for confounding factors such as blood pressure, resting heart rate, smoking status, Type 2 diabetes, previous myocardial infarction, LDL levels, and alcohol consumption. Their findings included a 66% risk reduction [HR 0.34 (0.16 – 0.71), $p = 0.004$] of dementia, a 65% risk reduction [HR 0.35 (0.14 – 0.90), $p = 0.03$] of Alzheimer's disease, a 63% risk reduction [HR 0.37 (0.18 – 0.75), $p = 0.005$] of sudden cardiac death, and a 40% risk reduction [HR 0.60 (0.46 – 0.80), $p < 0.001$] of all-cause mortality.[38, 39]

Rheumatological and Immune-mediated Disease

A Dutch study of 34 patients diagnosed with either rheumatoid arthritis (RA) or ankylosing spondylitis (AS) reported decreased pain and stiffness in the RA ($p < 0.05$) and AS ($p < 0.001$) groups during 4 weeks of sauna therapy that was not sustained after the 4 weeks, with no changes in disease activity being detected in either group based upon range-of-motion scoring and serum levels of ESR (erythrocyte sedimentation rate).[44]

A Japanese single-group study of 44 patients diagnosed with fibromyalgia with or without another rheumatological disorder (i.e. systemic lupus erythematosus, systemic sclerosis, rheumatoid arthritis, Sjogren's syndrome, Behcet's disease or aortitis syndrome) reported subjective improvements in VAS (visual analogue scale) pain scores ($p < .001$), reduced symptoms based upon FIQ (fibromyalgia impact questionnaire) ($p < 0.001$), improved quality of life indicators on SF-36 (short form 36-item) questionnaire ($p < 0.01 - 0.05$) as well as objective findings of fewer number of tender points ($p < 0.01$) palpated on physical exam after 12 weeks of combined far infrared sauna and underwater exercise therapy.[68]

Two studies of patients diagnosed with chronic fatigue syndrome/ myalgic encephalomyelitis reported subjective improvements after repeated sauna. Soejima-2015 ($n = 10$) reported decreased fatigue ($p = .002$) on numerical rating scales and improved scores for anxiety ($p = .008$), depression ($p = .018$), fatigue ($p = .005$) and performance status ($p = .005$) on POMS (profile of mood states) questionnaire after 4 weeks of infrared sauna sessions.[46] Amano-2015

(n=15) noted 77.8% of participants receiving 8 weeks of regular far infrared sauna therapy improved in symptoms based upon SF-36 (short form 36-item), SRQ-D (brief self-rating questionnaire for depression) and STAI (state-trait anxiety inventory questionnaire) compared to 50% of participants in the control group, who chose not to undergo sauna therapy.[43]

Chronic Pain Syndromes

Two randomised controlled trials investigated the subjective effects of repeated sauna on chronic pain disorders. One New Zealand study (n=37) of patients diagnosed with chronic tension headaches reported a 44% reduction in headache intensity within 6 weeks of the sauna treatment arm, with mean change in headache intensity between sauna and control group being 1.27 points (95% CI 0.48-2.07; F=10.17; df=1,117; p=0.002).[36] The other Japanese randomised controlled trial of 46 patients with chronic pain disorders detected an increased likelihood of return to work 2 years post-sauna intervention (p<0.05) and decreases in anger scoring (on CMI, Cornell Medical Index) in the 4-week sauna-treated group compared to control group (4.5 +/- 1.1 to 2.2 +/- 1.6, p<0.001) who received same courses of behavioural/ rehabilitation/ exercise therapy without additional sauna therapy.[47]

Depression

One randomised controlled trial that investigated the effects of 4 weeks of sauna sessions on 28 patients diagnosed with mild depression reported improved somatic complaints (p<0.001), improved hunger scores (p<0.0001), and improved relaxation scores (p<0.0001) based upon subjective somatic complaint, depression, hunger and relaxation scoring in the sauna group as compared to the control group that received bedrest instead of sauna therapy. In this same study, plasma ghrelin concentrations and daily caloric intakes also changed in the sauna group compared to control group (*t= -2.32, p<.05 and *t = -2.65, p<.05, respectively) with *student two-tailed group t-test.[69]

Lungs and Airways

Two studies focused on the effects of infrared sauna on patients diagnosed with COPD (chronic obstructive pulmonary disease). One controlled trial (n= 20) reported improved FEF₅₀ (forced expiratory flow after 50% of expired forced vital capacity) in patients receiving 4 weeks of repeated sauna [+0.08 L/s (0.01 – 0.212 L/s)] versus a control group [-0.01 L/s (- 0.075 – 0.04 L/s)], p=0.019 that received usual medical care. No other changes in spirometry parameters or 6-minute walk test distances were detected between the two groups.[64] The second study involved a single group of male, ex-smoker COPD patients (n= 13) with the following findings after 4 weeks of sauna sessions: improved symptom scores (59.7 pts +/- 16.9 to 55.3 pts +/- 17.2 pts, p=0.002); decreased pulmonary artery pressures during exercise (p=.028); increased exercise times after sauna exposures (360 s +/- 107s to 392 s +/- 97s, p=0.032); and improved oxygen saturation during exercise (p=.022).[65]

The Thai randomised controlled trial (n=26) that investigated the effects of a 6-week rehabilitation sauna program on patients diagnosed with symptomatic allergic rhinitis reported improved peak nasal inspiratory flow rates (119.2 L/s +/- 46.4 to 161.9 L/s +/- 46.7, p=0.002) and improved FEV₁ (forced expiratory volume at 1 sec) (77.5% +/- 9.8% to 95.6% +/- 5.7%, p=0.002) in the sauna intervention group compared to a control group that received usual medical care. The researchers also examined HRV (heart rate variability) parameters but detected no significant difference between the sauna and control groups.[70]

Another randomised controlled trial studied common cold sufferers in Germany (n=157) sitting for 3 minutes fully winter-dressed in a Finnish sauna daily over 3 days breathing in piped “hot dry” sauna air versus control “cool dry” room temperature air while wearing a face mask. Only on day 2 assessment, a decrease in symptom severity scoring was detected in treatment versus control groups [- 1.0(-2.0 - -0.1), p=0.04, 95% CI] but this finding was not sustained through days 3,5, and 7 of study. Fewer doses of cold and flu medications were taken by the treatment group on day 1 of assessment [3% (1 – 9%) vs 15% (8-28%), p=0.01, 95%CI], compared to the control group.[37]

Athletes

Two small non-controlled interventional trials studied the physiological effects of repeat sauna in athletes. One study (n=7) reported that 30 minutes of daily post-exercise sauna bathing for ten days was associated with peaked expansion of plasma volume after 4 days (+17.8%, 90%CI: 7.4 – 29.3%), followed by a trend back to pre-sauna levels by days 7 – 10.[40] The other study (n=16) noted a mean post-sauna increase in axillary body temp 2.6°C (p<0.001) after first sauna versus a mean increase of only 1.9°C (p<0.002) after completing a 5 months course of sauna bathing. The researchers also noted post-sauna increases in mean venous pH by 0.8% (p<0.001), decreased mean base excess

by 20.3% ($p < 0.001$), increased mean venous O_2 by 53.3% ($p < 0.001$), increased mean Hb concentration in blood by 5.2% ($p < 0.001$), and right shift of oxygen-hemoglobin dissociation curve (decreased affinity – favours release of O_2 to tissues) after the first sauna with similar changes in specified parameters noted after a final sauna 5 months later ($p < 0.043$ – $p < 0.005$).[71]

Healthy Populations

Two small uncontrolled, single-gender studies reported reduced total cholesterol levels (4.50 +/- 0.66 mmol/L to 4.18 +/- 0.41 mmol/L, $p = 0.02$) and reduced LDL (low density lipoprotein) levels (2.71 +/- 0.47 mmol/L to 2.43 +/- 0.35, $p = 0.01$) in healthy men ($n = 16$) after 4 weeks of regular sauna activity involving 45 min sauna sessions[59] and reduced total cholesterol levels (4.47 +/- 0.85 mmol/L to 4.25 +/- 0.93 mmol/L, $p < 0.05$) and reduced LDL levels (2.83 +/- 0.80 mmol/L to 2.69 +/- 0.83 mmol/L, $p < 0.05$) in healthy women ($n = 9$) after 2 weeks of regular sauna activity involving 30-minute sauna sessions[61]. The same research group of both studies reported earlier findings of significant increases in heart rate, systolic blood pressure, growth hormone, adrenocorticotrophic hormone and cortisol levels along with significant decreases in diastolic blood pressure and plasma volumes after single and repeated sauna sessions in 20 women after 2 weeks of either 30-min sauna sessions or 45-min sauna sessions.[60, 72] Reductions in total and LDL cholesterol levels along with increased HDL (high density lipoprotein) cholesterol levels were reported in the 45-min sauna group. .

Another study of healthy men and women examined the skin physiology of regular sauna attenders ($n = 21$) compared to newcomer sauna attenders ($n = 20$) before and after sauna bathing. The investigators reported a decrease in NaCl (sodium chloride) sweat concentrations in the regular sauna group (~200 mmol/L +/- ~10 mmol/L to ~170 mmol/L +/- ~10 mmol/L, $p = .0167$) without any respective changes in the newcomer sauna group. Baseline values (pre-sauna) of forehead sebum level were 25% lower in the regular sauna group ($p < .05$) compared with newcomer group but sebum levels decreased similarly in both groups post-sauna. Skin surface pH was generally measured to be lower in the regular sauna group but similar scales of pH elevation were recorded for both groups during and after sauna activity.[73]

Detoxification

Populations burdened with toxicants were the subject of two studies. Both entailed multimodal therapies with sauna as a prominent but not sole intervention and both demonstrated improved self-assessed quality of life measures. [41, 42] Ross-2012 ($n = 69$) documented improved post treatment SF-36 (short form 36-item health survey) scores in symptomatic policemen exposed to employment-related drugs and toxicants compared to pre-treatment scores (with 2-tailed student t- test paired scores and Wilcoxon matched pairs test and sign test, $p < 0.001$), across all subscales after 4 -6 weeks of infrared sauna sessions with up to 4 hours of sauna bathing daily. The FASE (Foundation for Advancements in Science and Education) 50-item and neurotoxicity symptom questionnaires further revealed fewer “poor physical health” days (9.3 vs 1.8 days, $p < 0.001$); fewer “sick days” (2.0 vs 0.3 days, $p < 0.001$); more sleep hours (5.8 vs 7.6 h, $p < 0.001$); and lessened neurotoxicity scoring (65.5 +/- 24.8 vs 14/6 +/- 11/5 points, $p < 0.001$).[42]

The other sauna detoxification study was a randomized controlled trial ($n = 36$) of symptomatic individuals with elevated levels of lipophilic toxicants, comparing two separate sauna interventions with a control group: I) steam sauna with oral and intravenous supplements, II) dry sauna with substitute placebo oral and intravenous interventions, III) no sauna, no oral, and no intravenous interventions. Using multivariate analysis of variance (MANOVA) methods, several somatic well-being scores improved in both treatment groups I & II, as compared to group III with Duncan post-hoc test suggesting significant differences between Group I and Group III ($p < 0.01$) and between Group I and II ($p < 0.05$). No differences however were seen between Group II and III ($p = 0.21$) and no significant changes in neuropsychological testing scores ($p > 0.10$) or serum concentrations of selected organochlorides ($p > 0.10$) were reported between any of the groups. [41]

Spermatogenesis

One longitudinal time-course study examined the effects of Finnish sauna activity on male sperm and fertility measures in 10 healthy men. After 3 months of repeated sauna (15-min saunas twice weekly), the investigators reported reduced sperm counts (93 +/- 27.0 x 10^6 vs 223 +/- 52.8 x 10^6 , $p < 0.001$); reduced sperm concentrations (31 +/- 13.1 x 10^6 /ml vs 89 +/- 29.3 x 10^6 /ml, $p < 0.001$); fewer motile sperm (36.1 +/- 3.6 % vs 58.0 +/- 7.6 %, $p < 0.01$); abnormal sperm parameters [decrease in normal histone-protamine replacement ($p < 0.05$), abnormal chromatin

condensation ($p < 0.05$), altered mitochondrial function ($p < 0.01$); up-regulation of various heat-stress genes [HIF-1 α ($p < 0.001$), KDR ($p < 0.001$), FLT1 ($p < 0.001$), VEGF ($p < 0.001$)] and up-regulation of HSPs (heat shock proteins) and HSFs (heat shock factors) [HSP90 ($p < 0.001$), HSP70 ($p < 0.001$), HSF1 ($p < 0.001$), HSF2 ($p < 0.001$), HSFY ($p < 0.001$)]. However, all specified changes reverted back to normal 6 months after ceasing sauna activity and no significant changes in plasma sex hormones from baseline were detected directly post-sauna or after 3 or 6 months.[27]

Adverse Side Effects

Of the 40 included studies, only eight reported any adverse symptoms from sauna bathing. Six studies recorded adverse effects graded as mild, meaning symptoms of complaint were noted which did not alter the study protocol or incur dropouts to the study. Mild heat discomfort was the major complaint.[40, 42, 44] Other mild complaints noted in one infrared sauna study of heart failure patients ($n=149$) included symptomatic low blood pressure, hypovolemia, polyurination, weight loss, and questionably, acute bleeding after a tooth extraction. [35] Another study of patients with peripheral arterial disease ($n=21$) reported transient leg pain in one participant during a first infrared sauna session with the pain improving after completing a few sauna sessions and disappearing altogether by the end of the 6-week study.[62] Pach-2010 reported coughing in 3 of 157 Finnish-style sauna participants, stimulated by the placement of a face mask in both intervention and control groups, with different temperatures of air piped through the masks of the respective groups.[37]

Two studies recorded moderate adverse effects, defined as symptom complaints that led to dropout of study participants or led to changes in study protocols. One study, involving fifteen women diagnosed with chronic fatigue syndrome/myalgic encephalomyelitis, reported enough heat intolerance in “most” of the participants such that the investigators reduced the temperature of the infrared sauna intervention from 60°C to 45°C to finish conducting the study.[43] Another infrared sauna study (randomized controlled trial) of chronic pain patients ($n=46$) reported 2 patients dropping out of the treatment arm due to acute bronchitis and claustrophobia experienced in the sauna room.[47] None of the included studies reported severe adverse effects involving the need for emergency medical services.

Table 1: Cardiovascular Disease (CVD) – Related Sauna Studies

Study Characteristics			Study Sample		Intervention		Comparators		Health Effects	Adverse Side Effects
Author & Year	Level of Evidence	Design	Pop/ Country	N	Sauna Type	Duration	Comparator/ Controls	Outcome Measures	POSITIVE/ NEGATIVE/ NEGLIGIBLE	None/Mild/ Moderate/ Severe
2016 – Tei et al[35]	I	RCT – Multi-centre	Advanced CHF/ Japan	149	FIR	2 weeks	Control group – standard medical care	6MWD (6 min walking distance), CTR (cardio-thoracic ratio) on chest X-ray, NYHA class, plasma BNP levels.	POSITIVE- Improved 6MWD (p<.05), reduced CTR on CXR (p<.05), and improved NYHA classification (p<.05) compared to control group	Mild- decreased BP, hypovolemia, polyurination, decreased body wt
2011 – Fujita et al[49]	I	RCT	CHF/ Japan	40	FIR	4 weeks	Control group- standard medical care	Body weight, BP, cardio-thoracic ratio (CTR) on chest X-ray, LVEF on ECHO, fasting plasma levels of BNP, uric acid, hydro-peroxide, nitrate, nitrite.	POSITIVE- Sauna group with reduced concentration of hydroperoxide (p<0.001); reduced BNP levels (p<0.001); increased nitric oxide metabolites (p<0.05).	None
2011 – Kuwahata et al[50]	I	RCT	CHF/ Japan	54	FIR	4 weeks	Control group – standard medical care	Body weight, BP, HR, CTR on chest X-ray, standard ECHO parameters, fasting plasma levels of catechol-amines and BNP; and HRV (heart rate variability) parameters	POSITIVE- Mean HR decreased (p<0.05) in sauna group compared to control group. High frequency component of HRV in setting of beta blockade improved.	None
2010 – Shinsato et al[62]	I	RCT	PAD/ Japan	21	FIR	6 weeks	Control group – standard medical care	Leg pain (using VAS), ABI (ankle-brachial index), 6MWD (6-min walking distance), PCR-CD34+ progenitor gene expression levels in peripheral blood mono-nuclear cells, serum levels of VEGF (vascular endothelial growth factor), nitrate and nitrite.	POSITIVE- Decrease in leg pain scores (p<0.05), increase in 6MWD (p<0.01), improved ABI (p<0.01), 2-fold increase in mRNA CD34/GAPDH gene expression levels (p=.015), increases in serum nitrate and nitrite levels (p<.05, p<.05) in sauna group compared to control group.	Mild- transient leg pain during sauna but resolved after a few sessions
2008 – Miyata et	I	RCT	CHF/ Japan	188	FIR	2 weeks	Control group- standard medical	BP, HR, body weight, body temp, CTR (cardio-thoracic	POSITIVE- BP and CTR decreased in both	None

al[51]							care	ratio) on chest X-ray, usual ECHO parameters, and fasting plasma BNP.	groups (sauna p<.01, p<0.001; control p<.05, p<.05). Body wt decreased (p<.0001); LVEF on ECHO increased (p<.0001); plasma BNP decreased (p<.001) in sauna group compared with control group.	
2004 – Kihara et al[53]	I	RCT	Cardiac Arrhythmias, CHF/ Japan	30	FIR	2 weeks	Control group placebo intervention - supine on a bed in a temp-controlled room at 24°C for 45 min.	Self-assessed quality of life questionnaire, 24-hr ambulatory ECG recordings with HRV analysis (std deviation of mean RR intervals), CTR (cardiothoracic ratio) by chest X-ray, usual ECHO parameters, plasma concentrations of catecholamines, ANP, BNP.	POSITIVE- Fewer PVCs (p<.01), fewer couplets (p<.05), fewer episodes of VT (p<.01), decreased CTR (p<.05), increased HRV variability (p<.01), and lowered serum levels of BNP (p<.01) in sauna treatment group compared to control group.	None
2004 – Masuda et al[56]	I	RCT	Increased CVD Risk/ Japan	28	FIR	2 weeks	Control group placebo intervention - supine on a bed in a temp-controlled room at 24°C for 45 min.	Body wt, HR, BP, HCT, fasting plasma lipid profile and glucose, urinary levels 8-epi-prosta-glandin F _{2α}	POSITIVE- Systolic BP (p<.05) and urinary 8-epi- prostaglandin F _{2α} levels (p<.001) significantly lower in sauna group compared to control group.	None
2016 – Laukkanen et al[39]	II	Pro-spective cohort study	Middle-aged males/ Finland	2315	Finnish	20.7 years	Frequency and duration of sauna bathing: 1 time/wk, 2-3 time/wk, 4-7 times/wk	Incidence dementia/ Alzheimer's disease and other CVD-related outcomes	POSITIVE- Sauna bathing 4 -7 times a week associated with 66% risk reduction (hazard ratio 0.34, 95%CI) in developing dementia or Alzheimers compared with 1 time/week.	None
2015 – Laukkanen et al[38]	II	Pro-spective cohort study	Middle-aged males/ Finland	2315	Finnish	20.7 years	Frequency and duration of sauna bathing: 1 time/wk, 2-3 time/wk, 4-7 times/wk	Incidence of sudden cardiac death, fatal coronary heart disease, fatal CVD, and all-cause mortality	POSITIVE- Sauna bathing 4-7 sessions weekly associated with 40 % reduction in all-cause mortality compared with 1 session weekly, (hazard ratio 0.60,95%CI,0.46-0.80, p<.001).	None
2013 – Sobajima et al[67]	II	Controlled clinical study	IHD with total coronary occlusion/ Japan	24	FIR	3 weeks	Control group - standard medical care	Myocardial perfusion scintigraphy with adenosine, flow-mediated vaso-dilation of brachial artery, treadmill exercise stress testing and expression of CD34-positive	POSITIVE- Improved indices of defect reversibility on myocardial perfusion scans (p<.01); extended treadmill times (p<.01), improved flow-	None

								bone marrow-derived cells	mediated dilation of brachial artery (p<0.05) after sauna therapy compared to control group.	
2003 – Sugahara et al[54]	II	Single group clinical study	Infants-VSD and CHF/ Japan	12	FIR	4 weeks	No control group	Core body temp, HR, BP, usual ECHO parameters including VSD measurements with colour doppler, 24h urine nitrate and nitrite levels	POSITIVE- Decrease in VSD shunt flow ratio (p<.05), increase in 24h urine nitrite and urine nitrate levels (p<.05, p<.05); Surgical repair not necessary for 9/12 (75%) infants.	None
2012 – Ohori et al[48]	III	Single group clinical study	CHF/ Japan	41	FIR	3 weeks	No control group	6MWT (6-min walk test); standard ECHO parameters; plasma levels of BNP, nor-epinephrine and circulating CD34+ cells; flow-mediated dilation (FMD) of the brachial artery.	POSITIVE- increased LVEF (left ventricular ejection fraction), p=.023; reduced levels of norepinephrine and BNP, p=.015 and p=.035; increased 6MWT, p<.001; improved FMD, p<.001; increased CD34+ counts, p=.025	None
2010 – Beever[45]	III	Single group – sequential, longitudinal, interrupted time series	Type 2 Diabetes/ Canada	15	FIR	3 months	No control group	SF-36 (36-item short form health survey) and VAS (visual analogue scales)	POSITIVE- Improved stress (p=.042), fatigue (p=.014), and general health (p=.037) on SF-36.	None
2009 – Kihara et al[66]	III	Retro-spective cohort study	CHF/ Japan	129	FIR	5 years	Control group - standard medical care	Episodes of cardiac death, cardiac events, and re-hospitalisations due to CHF.	POSITIVE- 8/64 patients died in sauna therapy group vs 12/65 patients in control group (12.5% vs 18.5% mortality rate); Rehospitalization due to worsening CHF occurred in 20/64 (31.3%) patients in sauna group vs 44/65 (68.7%) patients in control group (p<0.01); 38% reduction in cardiac event rate in sauna therapy group compared to control group.	None
2007 – Tei et al[74]	IIII	Single group clinical study/	PAD/ Japan	20	FIR	10 weeks	No control group	Leg pain using VAS (visual analogue scale), 6MWD (6 min walking distance), ABI (ankle/	POSITIVE- Pain scores decreased, 6MWD improved, ABI improved, increase in visible collateral	None

		pilot trial						brachial index), leg blood flow with doppler laser imaging, digital subtraction angiography	vessels in ischaemic legs with digital subtraction angiography observed after sauna therapy ($p < 0.01$ for all).	
2005 – Miyamoto et al[52]	III	Single group clinical study/ pilot trial	CHF/ Japan	15	FIR	4 weeks	No control group	Body wt, BP, HR; Self-assessed quality of life questionnaire; 6MWT (6 min walk time); peak VO2 on bicycle ergometer; CTR (cardio-thoracic ratio) on chest X-ray; usual ECHO parameters, plasma BNP, catecholamines; no. of hospitalisations one-year post sauna intervention	POSITIVE- Decreased SBP ($p < .05$), improved CTR ($p < .05$), improved LVEF on ECHO ($p < .05$), increased 6MWT ($p < .05$), decreased plasma norepinephrine and epinephrine levels ($p < .01$, $p < .05$) with sauna intervention. Reduced no. of hospitalisations ($p < .01$) one-year post sauna intervention.	None
2003 – Biro et al[57]	III	Clinical study with control group	Obesity, T2DM, Smoking, Hypercholesterolemia, HTN/ Japan	35	FIR	2 weeks	10/35 control group without any lifestyle diseases	Body wt, HR, BP, HCT; fasting serum lipid profile, glucose, uric acid levels; resting arterial diameter; flow mediated dilatation of brachial artery on doppler USS; plasma ghrelin and serum leptin levels.	POSITIVE- Decreased body wt ($p < .05$), SBP and DBP ($p < .01$, $p < .05$), FBG ($p < .05$); Improved flow mediated dilatation of brachial artery ($p < .001$) in sauna group but results compared to control not presented.	None
2002 – Kihara et al[55]	III	Clinical study with control group	CHF/ Japan	30	FIR	2 weeks	10/30 control group – standard medical care	Self-assessed quality of life questionnaire; HR, BP; fasting plasma levels of catecholamines, ANP, BNP, thiobarbituric acid-reactive substances, TNF-alpha; CTR (cardio-thoracic ratio) on chest X-ray; usual ECHO parameters; brachial artery diameter and flow-mediated dilation using doppler ultrasound.	POSITIVE- Decreased SBP ($p = .019$), decreased CTR on CXR ($p = .002$), decreased LVEDD (left ventricular end-diastolic dimension) on ECHO ($p = .047$), decreased plasma BNP levels ($p = .005$), improved flow-mediated dilation of brachial artery on doppler USS ($p = .0006$) in sauna group compared to control.	None

2001 – Imamura et al[58]	III	Clinical study with control group	Increased CVD Risk/ Japan	35	FIR	2 weeks	Control group 10/35 without any CVD risk factors	Body wt, HR, BP; fasting serum levels of HCT, Lipid profile, uric acid, glucose, thiobarbituric acid-reactive substances; flow mediated dilation of brachial artery using doppler USS; nitroglycerin-induced flow mediated dilation of brachial artery using doppler USS.	POSITIVE- SBP and DBP reduced (p<.01, p<.05); body wt reduced (p<.05); fasting glucose levels decreased (p<.05); %flow mediated dilation of brachial artery improved (p<.001) in sauna group but no statistical report of comparisons with control group.	None
--------------------------	-----	-----------------------------------	---------------------------	----	-----	---------	--	---	--	------

Table 1 Abbreviations:

CVD = cardiovascular disease; CHF = congestive heart failure; IHD = ischaemic heart disease; PAD = peripheral arterial disease; FIR = far infrared sauna; VSD = ventricular septal defect; NYHA = New York Heart Association grading for CHF; Temp = body temperature; HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; wt = body weight; ECHO = echocardiogram; VAS = visual analogue scale; FBG = fasting blood glucose; BNP = B-natriuretic peptide; HCT = haematocrit.

Table 2: Sauna Studies of Rheumatological Disease/ Chronic Pain/ Depression

Study Characteristics			Study Sample		Intervention		Comparators		Health Effects	Adverse Side Effects
Author & Year	Level of Evidence	Design	Pop/ Country	N	Sauna Type	Duration	Comparator/ Controls	Outcome Measures	POSITIVE/ NEGATIVE/ NEGLIGIBLE	None/ Mild/ Moderate/ Severe
2015 – Kanji et al[36]	I	RCT	Chronic Tension Headache / New Zealand	37	Multiple types - sauna voucher cards	8 weeks	Control group received advice and education	NPRS (numeric pain rating scale), BDI (Beck Depression Inventory), HDI (Headache Disability Index)	POSITIVE- 44% reduction in HA intensity in 6 weeks of treatment arm. Mean change in headache intensity between sauna and control group = 1.27 points (95% CI 0.48-2.07; F=10.17; df=1,117; p=0.002).	None
2005 – Masuda et al[47]	I	RCT	Chronic Pain/ Japan	46	FIR	4 weeks	Control group received same course of behavioural counselling, CBT, rehabilitation and exercise therapy	VAS for pain; pain behaviour assessment by researchers with 11-item questionnaire; Zung SDS (self-rating depression scale); anger scoring with CMI (Cornell Medical Index); sleep quality with simple 0-10 scoring;	POSITIVE- Increased likelihood of return to work 2 years later (p<0.05); decrease in anger scoring in sauna group compared to control (4.5 +/- 1.1 to 2.2 +/- 1.6, p<0.001).	Moderate- 2 patients excluded -could not tolerate sauna - acute bronchitis and claustrophobia

								degree of satisfaction of treatments with simple numerical scoring; return to work 2 years post-intervention		
2005 – Masuda A, Nakazato, M et al[69]	I	RCT	Mild Depression/ Japan	28	FIR	4 weeks	Control group received placebo – 45 min bedrest at 24°C and post-rest shower in addition to same rehab programs, physical therapy, occupational therapy.	Somatic complaints with CMI (Cornell Medical Index); Zung SDS (self-rating depression scale); VAS for hunger and relaxation; plasma levels of ghrelin, glucose, catechol-amines; daily caloric intake.	POSITIVE -Improved somatic complaints (p<0.001), improved hunger scores (p<.0001), and improved relaxation scores (p<.0001) in sauna group compared to control group. Plasma ghrelin concentrations and daily caloric intake increased in sauna group (*t= -2.32, p<.05 and *t = -2.65, p<.05, respectively);*t = student 2-tailed t-test.	None
2009 – Oosterveld et al[44]	III	2 single group (side-by-side) Intervention pilot trials	Rheumatoid Arthritis (RA) and Ankylosing spondylitis (AS)/ The Netherlands	34	FIR	4 weeks	No control group; two groups receiving same sauna intervention	VAS, EPM-ROM (Escola Paulista de Medicina range of motion), DUTCH-AIMS (Dutch arthritis impact measurement scales), BASMI (Bath Ankylosing Spondylitis functional index of range of motion), BASDAI (Bath Ankylosing Spondylitis disease activity index); serum ESR	POSITIVE – Pain and stiffness decreased in RA (p<0.05) and AS (p<0.001) groups during sauna sessions only.	Mild - 12 -24% scoring uncomfortable on well-being scores during beginning of sauna
2015 – Amano et al[43]	III	Clinical study with control group –pilot trial	Females with Chronic Fatigue Syndrome / Myalgic Encephalomyelitis/ Japan	15	FIR	8 weeks	6/15 chose not to undergo sauna intervention	SF-36 survey; SRQ-D (brief self-rating questionnaire for depression); STAI (state-trait anxiety inventory questionnaire)	POSITIVE - 7/9 in sauna group improved during sessions; 4/9 were still improved at follow-up 9 -40 months afterwards; 2/9 non-responders. 3/6 controls receiving usual treatment improved at follow-up.	Moderate - heat intolerance in most participants, protocol changed.
2015 – Soejima et al[46]	III	Single group clinical study	Chronic Fatigue Syndrome (CFS)/ Japan	10	FIR	4 weeks	No control group	Numerical rating scales for fatigue and POMS (profile of mood states) questionnaire	POSITIVE – Decreased fatigue (p=.002), improved POMS scores for anxiety (p=.008), depression (p=.018), fatigue (p=.005) and performance status (p=.005) after sauna.	None

2011 – Matsumoto et al[68]	III	Single group clinical study	Females with Fibromyalgia and Auto-immune Disorders/ Japan	44	FIR	12 weeks	Sauna only one part of intervention; combined with underwater exercise therapy; no control group.	VAS-visual analogue scale; no. of tender pts on clinical exam; FIQ- fibromyalgia impact questionnaire; SF-36 quality of life questionnaire	POSITIVE- Reduced VAS pain scores (p<.001); fewer # of tender pts (p<0.01); reduced symptoms based upon FIQ (p<0.001); improved quality of life on SF-36 questionnaire (p< 0.01 – 0.05) after combined sauna + underwater exercise therapy.	None
-----------------------------------	-----	-----------------------------	--	----	-----	----------	---	--	--	------

Table 2 Abbreviations:

FIR = Far infrared sauna; ESR = erythrocyte sedimentation rate; VAS = visual analogue scale; CBT = cognitive behavioural therapy

Table 3: Airway Conditions and Repeated Sauna Therapy

Study Characteristics			Study Sample		Intervention		Comparators		Health Effects	Adverse Side Effects
Author & Year	Level of Evidence	Design	Pop/ Country	N	Sauna Type	Duration	Comparator/ Control	Outcome Measures	POSITIVE/ NEGATIVE/ NEGLIGIBLE	None/ Mild/ Moderate/ Severe
2013 – Kunbootsri et al[70]	I	RCT	Allergic Rhinitis/ Thailand	26	Thai/ Finnish	6 weeks	Control group received education and usual medical care	HRV, peak nasal inspiratory flow and usual spirometry parameters	POSITIVE – Reduced high-freq component (p=0.003), increased low-freq component (p=0.003), increased low freq: high freq ratio (p=0.003) in HRV analysis; peak nasal inspiratory flow improved (119.2 L/s +/- 46.4 to 161.9 L/s +/- 46.7, p=0.002); FEV ₁ (forced expiratory volume at 1 sec) improved (77.5% +/- 9.8% to 95.6% +/- 5.7%, p=0.002) in sauna group compared with control group.	None
2010 – Pach et al[37]	I	RCT – Single blinded	Coryza/ common cold symptoms / Germany	157	Finnish	3 days	Face mask breathing hot dry air at 90°C, 20% RH in treatment group; Face mask breathing cool, dry air at 24°C, 20% RH in control group.	Symptom severity scoring (0-10) on four different days; intake of common cold medications daily during week of intervention.	NEGLIGIBLE – On day 2 only, significant decrease in symptom severity in treatment vs control group [- 1.0(-2.0 - -0.1), p=0.04, 95% CI] but was not sustained through day 3,5,7 assessments. Less cold medication taken on day 1 only [3% (1 – 9%) vs 15% (8-	Mild – cough directly stimulated by face mask in both groups (2 in treatment group; 1 in control group).

									28%)] in treatment vs control group (p=0.01, 95%CI).	
2014 – Kikuchi et al[64]	II	Controlled intervention trial	COPD/ Japan	20	FIR	4 weeks	Control group received usual medical care	Spirometry parameters; 6MWT (6-minute walk test); modified Borg dyspnea scale; oxygen saturation;PR	POSITIVE – Between-group improvements in FEF ₅₀ (forced expiratory flow after 50% of expired forced vital capacity) in sauna group [+0.08 L/s (0.01 – 0.212 L/s)] vs control group [-0.01 L/s (- 0.075 – 0.04 L/s)], p=0.019.	None
2008 – Umehara et al[65]	III	Single group intervention, pilot study	Male COPD Ex-smokers/ Japan	13	FIR	4 weeks	No control group	BP, PR, body wt, body temp; usual ECHO parameters; exercise tolerance by bicycle ergometer; SGRQ (St. George’s Respiratory Questionnaire) symptom scores; plasma BNP, HCT, albumin before/after treatment.	POSITIVE – Decreased SBP and DBP (p=.002-.0002); improvements in RV function via increased pressure differential (p=.024); Pulmonary artery pressure during exercise decreased (p=.028); increased exercise time (360 s +/- 107s to 392 s +/- 97s, p=0.032); lowest SpO ₂ during exercise increased (p=.022); symptom scores improved (59.7 pts +/- 16.9 to 55.3 pts +/- 17.2 pts, p=0.002) after sauna.	None

Table 3 Abbreviations:

COPD = chronic obstructive pulmonary disease; FIR = far infrared sauna; PR = pulse rate; HR = heart rate; BP = blood pressure; SBP = systolic blood pressure; DBP = diastolic blood pressure; wt = weight; temp = body temperature; HRV = heart rate variability; freq = frequency; RH = relative humidity; ECHO = echocardiogram; BNP = B-natriuretic peptide; E/LFTs = electrolytes with liver function tests.

Table 4: Repeated Sauna and Athletes

Study Characteristics			Study Sample		Intervention		Comparators		Health Effects	Adverse Side Effects
Author & Year	Level of Evidence	Design	Pop /Country	N	Sauna Type	Duration	Comparator/ Controls	Outcome Measures	POSITIVE/ NEGATIVE/ NEGLIGIBLE	None/ Mild/ Moderate/ Severe
2014 – Stanley et al[40]	III	Single group, Interrupted time series study	Elite Athletes – Males/ Australia	7	Finnish	10 days	No control group	Plasma volume changes (calculated from Hb readings), hydration status (using urine SG by digital refractometer; ergometer exercise performance measures; HRV.	POSITIVE – Post exercise sauna bathing increased plasma volume after 4 days of intervention (p<0.01).	Mild – comments of “hot and very uncomfortable, but tolerable” per thermal comfort survey conducted every 5 min during sauna sessions.
2012 – Zinchuk & Zhadzko[71]	III	Single group inter-ventional study	Male Elite Athletes/ Belarus	16	Finnish	5 months	No control group	Axillary temp; venous blood gas analysis; lipid peroxidation and free radical processes by UV and fluorescence analysis of plasma and RBCs; anti-oxidant estimation by α -tocopherol fluorescence analysis of plasma and RBC catalase activity; nitric oxide metabolism by spectrophotometric methods – plasma nitrate and nitrite levels.	POSITIVE – Increased axillary body temp 2.6°C (p<0.001) after first sauna and 1.9°C (p<0.002) after course of sauna; increased pH by 0.8% (p<0.001), decreased base excess by 20.3% (p<0.001), increased venous O ₂ by 53.3% (p<0.001), increased Hb concentration in blood by 5.2% (p<0.001), right shift of oxy-Hb dissociation curve (decreased affinity – favours release of O ₂ to tissues) after 1 st sauna; similar changes after final sauna (p<0.043 – p< 0.005);	None

Table 4 Abbreviations:
RH = relative humidity; Hb – haemoglobin; SG = specific gravity; HRV = heart rate variability; temp = body temperature; O₂ = oxygen; ROS = reactive oxygenated species; RBCs = red blood cells or erythrocytes.

Table 5: Sauna Studies of Healthy Populations

Study Characteristics			Study Sample		Intervention		Comparators		Health Effects	Adverse Side Effects
Author & Year	Level of Evidence	Design	Pop/ CountryCountry	NN	Sauna Type	Duration	Comparator/ Control	Outcome Measures		
2010 – Pilch, Szygula et al[60]	II	Two group clinical Inter-ventional study	Healthy females/ Poland	20	Finnish	2 weeks	Group 1 intervention-sauna x 30min; Group 2 intervention – sauna x 45 min	HR, SBP, DBP, tympanic temp, rectal temp, wt; exhaled air analysis for O2 uptake, CO2 exhalation, respiratory quotient; blood analysis for Hb, HCT, calc plasma volume changes, lipid panel, free fatty acids, total free fatty acids – all measured before/after 1 st sauna and final sauna.	POSITIVE -Reduced total cholesterol (p<0.05), reduced LDL cholesterol (p value unclear), increased HDL cholesterol (p<0.05) claimed (reported numbers do not agree) in group 2 after repeat sauna.	None
2008 – Kowatzki et al [73]	II	2-group side-by-side clinical inter-ventional study	Healthy men and women/ Germany	41	Finnish	Minimum one month of weekly sauna use in 'regular sauna group'.	Two groups receive same 2-session sauna intervention: Group 1 – 'regular sauna group' before intervention Group 2 – 'newcomer sauna group' with no prior sauna 3 months before intervention.	TEWL (trans epidermal water loss); stratum corneum hydration; skin erythema; skin surface pH; surface sebum content; ionic concentration of NaCl in sweat.	POSITIVE – Baseline values (pre-sauna) of forehead sebum level 25% lower in regular sauna group (p<.05); sebum levels decreased similarly in both groups; decrease in NaCl sweat concentration in regular sauna group only (~200 mmol/L to ~170 mmol/L, p=.0167); skin surface pH lower in regular sauna group but similar elevations with sauna activity.	None
2007 – Pilch et al[72]	II	Two group clinical inter-ventional study	Healthy Women/ Poland	20	Finnish	2 weeks	Group 1 intervention-sauna x 30min; Group 2	HR, BP, rectal and tympanic temp, body wt; blood Hb; calc plasma volume; serum levels of TSH, T3, T4, human	POSITIVE - Increased HR, increased SBP, decreased DBP and reduced plasma volumes after single and repeated sauna sessions in both groups (p< 0.005 – p<0.01).	None

							intervention – sauna x 45 min	growth hormone, ACTH, cortisol.	Increased secretions of growth hormone, ACTH, cortisol after single and repeated sauna sessions in both groups ($p < 0.01$ – $p < 0.05$).	
2014 – Gryka et al[59]	III	Single group clinical study	Healthy males/ Poland	16	Finnish	4 weeks	No control group	Body mass, HR, Body skinfold thickness, blood lipid profiles and plasma volumes	POSITIVE – Reduced total cholesterol (4.50 ± 0.66 mmol/L to 4.18 ± 0.41 mmol/L, $p=0.02$) and LDL levels (2.71 ± 0.47 mmol/L to 2.43 ± 0.35 , $p=0.01$) after 10 sessions of sauna over 2 weeks – returned to baseline after 2 weeks without sauna. No significant changes in HDL levels.	None
2014 – Szygula, Pilch et al[61]	III	Single group clinical study	Healthy females/ Poland	9	Finnish	2 weeks	No control group	Tympanic temp, rectal temp, wt; plasma levels of Hb, HCT, lipid panel and free fatty acids.	POSITIVE - Reduction in total cholesterol (4.47 ± 0.85 mmol/L to 4.25 ± 0.93 mmol/L, $p < 0.05$) and LDL levels (2.83 ± 0.80 mmol/L to 2.69 ± 0.83 mmol/L, $p < 0.05$) after repeated sauna.	None

Table 5 Abbreviations:

HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; temp = body temperature; wt = body weight; Hb = haemoglobin; HCT = haematocrit; calc = calculated; lipid panel = total cholesterol, triglycerides/ triacylglycerols, high-density lipoproteins, low-density lipoproteins; NaCl = sodium chloride.

Table 6: Repeat Sauna Therapy and Detoxification

Study Characteristics			Study Sample		Intervention		Comparators		Health Effects	Adverse Side Effects
Author & Year	Level of Evidence	Design	Pop / Country	N	Sauna Type	Duration	Comparators/ Controls	Outcome Measures	POSITIVE/ NEGATIVE/ NEGLIGIBLE	None/ Mild/ Moderate/ Severe
2009 – Huppe et al[41]	I	RCT	Symptomatic patients with elevated serum levels of lipophilic toxicants (PCBs, DDT, DDE)/ Germany	36	Two types: Sauna I (65°C, 70% RH) and Sauna II (50°C, 30% RH)	4 weeks	3 groups: I - Steam sauna + physiotherapy + oral and intravenous detox supplements II - Dry sauna + physiotherapy + placebo oral and intravenous supplements III - No sauna or oral/IV treatment	Psychologist (blinded)-assessed and self-assessed scoring using validated tools: somatic symptom complaint list scoring – Beschwerden-Liste 24-item questionnaire; general depression scoring using ADS-L/ CES-D 20-item questionnaire; SF-36 quality of life questionnaire; neuropsychological processing speed with GT-MT/ZVT scoring; concentration with ‘attention test d2’; memory power and speed with WL-N and WL-G scoring; serum levels of PCB congeners x 3, HCB, DDT, DDE.	POSITIVE - Improvements in several somatic well-being scores in both treatment groups I & II, as compared to group III with Duncan post hoc test suggesting differences between Group I and Group III (p<0.01) and between Group I and II (p<0.05) but no difference between Group II and III (p=0.21); No significant changes in neuropsychological testing scores between the groups (p>0.10); No significant changes in serum concentrations of selected organochlorides between the groups (p>0.10).	None
2012 – Ross & Sternquist[42]	III	Retro-spective chart review and follow-up surveys	Symptomatic police officers with employment-related drug and toxicant exposures/ U.S.A.	69	Infrared Sauna – full spectrum (160°F)	4 -6 weeks	No control group	RAND® SF-36 (36-item quality of health survey); FASE 50-item survey of symptoms and sleep; 13-item neurotoxicity questionnaire; MMSE; and review of daily medical records during therapy.	POSITIVE - Improved post treatment SF-36 scores compared to pre-treatment scores (with 2-tailed student t-test paired scores + Wilcoxon matched pairs test and sign test, p< 0.001), across all subscales; Comparing pre and post completion of program: fewer “poor physical health” days (9.3 vs 1.8 days, p<0.001); fewer “sick days” (2.0 vs 0.3 days, p<0.001); more sleep hours (5.8 vs 7.6 h, p<0.001);	Mild – heat discomfort

										lessened neurotoxicity scoring (65.5 +/- 24.8 vs 14/6 +/- 11/5 points, p<0.001); no changes in MMSE (29.3 vs 29.1 points, p=0.122).
--	--	--	--	--	--	--	--	--	--	---

Table 6 Abbreviations:

FASE = Foundation for Advancements in Science and Education; MMSE = Mini-Mental State Examination; ADS-L/CES-D = Allgemeine Depressions Skala/Centre for Epidemiological Studies Depression Scale; GT-MT/ZVT = German Trail-Making Test/Zahlenverbindungstest; WL-N = Wortliste Niveau memory power test; WL-G = Wortliste Geschwindigkeit memory speed test; PCB = polychlorinated biphenyls; HCB = hexachlorobenzene; DDT = Dichlorodiphenyltrichloroethane; DDE = p-dichlorodiphenylethylene

Table 7: Repeated Sauna and Male Fertility

Study Characteristics			Study Sample		Intervention		Comparators		Health Effects	Adverse Side Effects
Author & Year	Level of Evidence	Design	Pop/Country	N	Sauna Type	Duration	Comparator /Controls	Outcome Measures	POSITIVE/ NEGATIVE/ NEGLIGIBLE	None/ Mild/ Moderate/ Severe
2013 – Garolla et al[27]	II	Single group, longitudinal time-course study	Healthy males/ Italy	10	Finnish Sauna	3 months	No control group	Pre, post-intervention, post 3 months, post 6 months intervention: semen analysis; plasma sex hormone levels (LH, FSH, testosterone, inhibin); sperm parameters; sperm chromatin structure analysis; sperm apoptosis; sperm heat stress gene expression with quantitative real-time PCR analysis: HIF-1α, KDR, FLT1, VEGF, HSP90, HSP70, HSF1, HSF2, HSFY	<p>NEGATIVE - Post-intervention: lowered sperm count (93 +/- 27.0 x 10⁶ vs 223 +/- 52.8 x 10⁶, p<0.001); lowered sperm concentration (31 +/- 13.1 x 10⁶/ml vs 89 +/- 29.3 x 10⁶/ml, p<0.001); fewer motile sperm (36.1 +/- 3.6 % vs 58.0 +/- 7.6 %, p<0.01) with no differences noted by 6 months post end of sauna intervention.</p> <p>No significant changes in plasma sex hormones at any timepoints. Abnormal sperm parameters [decrease in normal histone-protamine replacement (p<0.05), abnormal chromatin condensation (p<0.05), altered mitochondrial function (p<0.01)]; up-regulation of heat-stress genes [HIF-1α (p<0.001), KDR (p<0.001), FLT1 (p<0.001),</p>	None

										VEGF (p<0.001)] and up-regulation of heat shock proteins/ factors [HSP90 (p<0.001), HSP70 (p<0.001), HSF1 (p<0.001), HSF2 (p<0.001), HSFY (p<0.001)] directly after sauna intervention but all changes completely reversed by 6 months post ceasing sauna activity.
--	--	--	--	--	--	--	--	--	--	---

Table 7 Abbreviations:

LH = luteinizing hormone; FSH = follicle stimulating hormone; PCR = polymerase chain reaction; HIF-1 α = hypoxia-inducible factor I alpha; KDR = kinase insert domain; FLT1 = fms-related tyrosine kinase; VEGF = vascular endothelial growth factor; HSP90 = heat shock protein 90; HSP70 = heat shock protein 70; HSF1 = heat shock factor 1; HSF2 = heat shock factor 2; HSFY = heat shock factor Y.

Discussion

Principal Findings

The findings of this review suggest frequent dry sauna bathing improves a variety of subjective and objective health parameters and that frequent Finnish sauna bathing is associated with improved outcomes such as reduced overall mortality and reduced incidence of cardiovascular events and dementia, at least in men.[38, 39] The most established clinical benefits of sauna bathing are associated with cardiovascular disease, yet there is also evidence to suggest that saunas, either Finnish-style or infrared, may benefit people with rheumatic diseases such as fibromyalgia, rheumatoid arthritis and ankylosing spondylitis, as well as patients with chronic fatigue and pain syndromes, chronic obstructive pulmonary disease and allergic rhinitis. Sauna bathing may also improve exercise performance in athletes, skin moisture barrier properties, and quality of life and is not associated with serious adverse events. There is not yet enough evidence to distinguish any particular health differences between repeat Finnish-style and repeat infrared sauna bathing.

Cardiovascular disease has clearly been a focus for sauna researchers since 2000 despite Finnish-style sauna being considered by some in the past as a contraindication for patients with CHF and other cardiovascular diseases, most likely because of perceived intolerance to the high temperatures. [1]. Nearly half (19 of 40) of the studies included in this review involved populations who had active cardiovascular disease or increased risk for cardiovascular disease, and all these studies demonstrated beneficial health effects. Seven of these 19 studies were randomized controlled trials (RCTs), with only one of them meeting the Cochrane criteria for an acceptably low risk of bias. This particular multi-centre RCT (n=149) reported improvements in all outcome measures except B-type natriuretic peptide (BNP) levels (namely longer 6-minute walking distance, reduced cardio-thoracic ratio on chest X-ray, improved NYHA- New York Health Association- classification) in the infrared sauna-treated congestive heart failure group compared to control over only 2 weeks of intervention.[35]

While sauna bathing appears to show promise as a lifestyle intervention for cardiovascular disease, a majority of the cardiovascular disease-related sauna studies (16 of 19) were conducted by the same core Japanese research group and affiliates who employed “Waon therapy”[74], which involved far infrared sauna bathing. These Waon therapy studies used similar outcome measures and mostly involved hospitalised patients, which might reflect some differences in health care systems and thresholds for hospitalisation. The use of primarily hospitalised patients in these studies also brings up issues of how applicable the findings may or may not be to outpatient populations.

Despite differences in sauna types, temperature, frequency and duration of interventions, the far infrared sauna studies involving cardiovascular disease and congestive heart failure patients suggest favourable outcomes that reinforce earlier findings of interventional Finnish sauna studies and cardiovascular disease.[75-79] This suggests that heat stress, whether induced by infrared or Finnish-style sauna, causes significant sweating that is likely to lead to hormetic adaptation and beneficial cardiovascular and metabolic effects. This is further supported by the two large observational studies that found striking risk reductions for sudden cardiac death (63%) and all-cause mortality (40%) as well as for dementia (66%) and Alzheimer’s disease (65%), in men who used a sauna 4 -7 times per week compared to only once per week.[38, 39] While these large cohort studies are based on calculated hazard ratios with adjustments for common cardiac risk factors, it has been pointed out that the association between sauna activity and health outcomes may be non-causal and that sauna use is merely an indicator of “healthy lifestyle” and other socioeconomic confounding factors.[80] Nevertheless, these findings point to the need for further study and serious consideration given to sauna bathing to address the ever-increasing individual, societal and financial burdens of cardiovascular disease as well as dementia-related conditions in aging populations.

Mechanisms of Action – Sauna Bathing

Several mechanisms of action have been proposed for the health effects of frequent sauna bathing. Exposure to heat increases cardiac output and reduces peripheral vascular resistance and induces other physiological changes in cardiovascular parameters such as decreased systolic and/or diastolic blood pressure[35, 51, 52, 55-58, 65, 72], increased HRV (heart rate variability)[50, 53, 70], improved cardiac function markers[35, 48, 50-53, 55, 67] and improved flow-mediated arterio- and vaso-dilatation of small and/or large blood vessels.[48, 55, 57, 58, 62, 63, 67] Regarding hormonal and metabolic models, reduced levels of epinephrine and/or norepinephrine[48, 52], increased levels of nitric oxide metabolites in blood[49, 62] and urine[54], decreased total and LDL (low density lipoprotein)

cholesterol levels[59-61], increased serum levels of growth hormone, adrenocorticotrophic hormone (ACTH), and cortisol[72], decreased fasting blood glucose levels[58], increased plasma ghrelin levels[69], and reduced urinary levels of prostaglandins (8-epi-prostaglandin F_{2α})[56] have been detected after regular sauna sessions. Together, these findings support complex multi-pathway end-organ effects on the central and autonomic nervous system, the peripheral vascular endothelium, the hypothalamus-pituitary-adrenal axis, as well as on the kidneys and the liver that are continuing to be documented.[1, 11, 28, 81]

The complexity of how sauna bathing may influence cardiovascular risk factors is suggested by the report of beneficial effects on total cholesterol and LDL (low density lipoprotein) cholesterol and conflicting results on HDL (high density lipoprotein) levels in healthy young men and women [59-61]. These findings, which need to be confirmed in larger studies with non-sauna control groups, may point to differences between Finnish and infrared saunas as they contrast with previous similarly-sized, yet better controlled studies of infrared sauna bathing in populations at increased risk of cardiovascular disease.[56-58]. These findings may also be compared to the metabolic effects of exercise in healthy populations which include improvements in both LDL and HDL lipid levels.[82]

While there are likely to be many mechanisms of action influencing the physiological effects of sauna bathing, it has been suggested that sauna bathing may induce a general stress-adaptation response that leads to 'hormetic adaptation' and the establishment of 'sauna fitness', possibly analogous to the hormetic adaptation responses of exercise. This is supported by newer, single-cell analysis methods that suggest sauna bathing increases generation of free radicals and reactive oxygenated species along with enhanced anti-oxidant activities via proposed nitric oxide (NO)-dependent processes in blood[71] and upregulation of specific HSPs (heat shock proteins) and HSFs (heat shock factors) in semen.[27] The two studies in athletes further support sauna's involvement in hormetic stress responses with the findings of plasma volume expansion after 4 days of daily post-exercise sauna bathing, followed by a trend back to pre-sauna levels by days 7 – 10 in one study[40], along with mean post-sauna increases in axillary body temperature of 2.6°C after a first sauna versus mean post-sauna increases of only 1.9°C after the last session of a 5-month course in the other study.[71] Additionally, increases in plasma lipid peroxidase levels and increases in free radical processes of RBCs, and decreases in plasma α-tocopherol (anti-oxidant) levels and decreases in RBC catalase activity after an initial sauna were not maintained after 5 months of regular sauna[71], suggesting that sauna bathing may upregulate antioxidant defences.

Improved adaptation to stress with regular sauna bathing may be further enhanced by excretion of toxicants through heavy sweating. Many industrial toxicants including heavy metals, pesticides and various petrochemicals may be excreted in sweat leading to an enhancement of metabolic pathways and processes that these toxic agents inhibit.[83] Sweat-induced excretion of toxic metals such as arsenic, cadmium, lead and mercury, has been reported with the rates of excretion matching or exceeding urinary routes.[84] There is also recent evidence that toxic chemicals and xenobiotics such as polybrominated diphenyl ether (PBDE) flame retardants, organochlorine pesticides, bisphenol-A (BPA), and phthalates may be excreted via induced sweating at rates that exceed urinary excretion.[85-88] The importance of sweat in excretion pathways has been further documented by sweat-patch technology used to monitor illicit drug use and is based on dozens of studies of the pharmacodynamics and pharmacokinetics of amphetamine, cocaine, cannabis, opiates and associated metabolites.[89, 90] While sweat-induced detoxification certainly occurs, studies using sauna for detoxification purposes report more favourable findings with subjective rather than objective measures. [42] [41] Further research on sauna-based detoxification is warranted as the excretory functions of skin via sweating or other active, passive inter- and/or transcellular, and transdermal pathways are complex and the role of frequent sweating to promote excretion and improve health is still poorly defined.[91]

In addition to having profound physiological effects, sauna bathing is reported to have beneficial psychological effects that are reflected in the many reports of improved well-being, pain tolerance and other self-assessed symptom-related scoring.[36, 37, 41-47, 52, 53, 62, 65, 68, 69, 74] The psychological impact of sauna bathing may be due to a combination of factors that include release of endorphins and other opioid-like peptides such as dynorphins[81, 92], forced mindfulness, psychological stress reduction, relaxation, improved sleep, time out from busy life schedules, placebo effects and other aspects of individual psychological and social interactions that likely occur around frequent sauna activity. While it is difficult to distinguish between the different factors that produce

positive psychological effects, such effects may enhance other physiological and metabolic benefits as they are likely to promote adherence to regular sauna activity.

Safety and Adverse Effects with Sauna

In the medical literature at large, there are reports of severe adverse effects from saunas that include dry sauna-induced burns,[93] myocardial ischemia (especially in patients with unstable coronary artery disease)[94], along with less frequent reports of syncope/falls[1], hypersensitivity pneumonitis ('sauna lung')[95], non-exertional heatstroke[96], rhabdomyolysis[93], ocular irritations[97], 'sauna stroke syndrome'[98] and death[99]. The risk of death from saunas was examined in retrospective population studies of frequent sauna users in Sweden and Finland, with the annual death rate from saunas being reported as 0.06 and 2 per 100,000 inhabitants respectively, with half or more of all these deaths involving the use of alcohol and a common risk factor of sauna-bathing alone .[99, 100]

In this review, adverse signs and symptoms of both Finnish-style and infrared sauna bathing were reported as mild to moderate heat discomfort and intolerance in 4 of the studies[40, 42-44], low blood pressure/ light-headedness in one study[35], transient leg pain in another study[62], airway irritation in two studies[37, 47] , and claustrophobia in one study[47], with no severe adverse symptoms reported in any studies. Detailed comparative analysis of adverse effects between studies was limited by small sample sizes, heterogeneity of sauna types and study design (many without control groups) and inconsistent reporting of adverse side effects within outcome measures. The highest intensity of adverse effects (moderate levels of heat intolerance) occurred in populations afflicted with chronic fatigue syndrome, chronic pain, rheumatoid arthritis and ankylosing spondylitis. As these conditions are all associated with inflammation and abnormal immune responses, it may be that the heat and/or increased sweating of sauna activity is modulating some of these responses. [43, 44, 47] The direct adverse effects of heat may also be responsible for the impairment of sperm counts, concentration and motility and up-regulation of heat stress-related genes reported in the sperm of 10 healthy men after a 3-month course of Finnish-style sauna.[27] While these findings are based upon one identified study of only 10 men, the findings are consistent with some earlier research on the effects of genital heat stress on semen quality [101-104]. All the deleterious sperm effects of the sauna intervention mentioned in this study were observed to revert back to 'normal' pre-sauna levels after 6 months of avoiding sauna activity.[27] While this supports current recommendations for men seeking to optimize fertility to avoid sauna-type activities[105], further research is required to determine if similar effects on sperm occur with lower temperature infrared sauna bathing or if sauna bathing has any effect on male fertility.

Strengths/ Limitations

To the best of our knowledge, this is the first systematic review to include both Finnish-style and infrared sauna studies. However, we did not include studies of steam sauna interventions and therefore may have overlooked some evidence of the effects of heat on health. Another limitation of this study is the inclusion of only English language, especially since sauna activity is frequent in non-English speaking countries. Furthermore, the quality of the reviewed studies was variable with many studies having small sample sizes, poorly described methodology, variable use of controls, differing types of sauna and sauna protocols, variable duration and frequency of sauna interventions and inconsistent mention of cooling therapies or rehydration protocols along with heterogeneous outcome measures. The great heterogeneity of studies makes meaningful comparisons across studies difficult and provides insufficient evidence to recommend specific temperature, frequency or duration of sauna bathing for any specific health outcome.

In the months since this systematic review was conducted, a number of new research findings have been published, analyzing various subsets of the same Finnish prospective cohort of over 2000 men who regularly sauna-bathed, initially aged 42-60 years old, followed over 20 years as part of the KIHD (Kuopio Ischemic Heart Disease) study, as detailed in two of the studies included in Table 1: Cardiovascular Disease (CVD) – Related Sauna Studies. These newer findings cite reduced risk of acute and chronic respiratory conditions[106], reduced risk of pneumonia[107], reduced serum levels of C-reactive protein (marker of systemic inflammation)[108] with more frequent sauna bathing, as well as reduced risk of hypertension[109] and additional improved all-cause mortality when jointly associated with cardiorespiratory fitness[110]. These findings add further support to the conclusions of this review.

Future Research Perspectives

With the rise of single cell analysis and 'omics' platforms of analysis such as metabolomics and transcriptomics, especially applied to sweat, blood, urine, saliva and other human biofluids, the ability to unravel the metabolic pathways at work during sauna or whole-body thermotherapy will certainly improve. Further study of these metabolic pathways might also help to elucidate the stress-related pathways of immune and inflammatory activity that may be involved in conditions such as chronic fatigue syndrome, chronic pain, rheumatoid arthritis and ankylosing spondylitis.

Studies examining heart rate variability (HRV) as an outcome assessment are increasing and further results may better inform the physiological models of what is thought to be happening with repeated sauna of either Finnish or infrared types. The concepts of hormetic stress and interrelating 'sauna fitness' or habituation to the physiological effects of repeated sauna activity might have implications for preventive or therapeutic targets in the future. Conducting more studies of repeated sauna in healthy but non-athletic participants may further help to elucidate the similarities and differences in metabolic pathways between repeated sauna activity and regular exercise. Further studies are also needed to distinguish between the health effects of Finnish saunas, which often involve brief periods of increased humidity and dramatic cooling interventions, compared to the lower temperature infrared saunas that typically do not have such variations.

Conclusions

Regular infrared and/or Finnish sauna bathing has the potential to provide many beneficial health effects, especially for those with cardiovascular-related and rheumatological disease, as well as athletes seeking improved exercise performance. The mechanisms for these effects may include increased bioavailability of NO (nitric oxide) to vascular endothelium, heat shock protein-mediated metabolic activations, immune and hormonal pathway alterations, enhanced excretions of toxicants through increased sweating and other hormetic stress responses.

Currently there is insufficient evidence to recommend specific types of sauna bathing for specific clinical conditions. While regular sauna bathing appears to be well-tolerated in the clinical setting with only minor and infrequent adverse effects reported, further data on the frequency and extent of adverse effects is required. Further studies are also required to explore the mechanisms by which sauna bathing exerts physiological, psychological and metabolic effects, as well as to better define the benefits and risks of distinct types of saunas and the optimal frequency and duration of sauna bathing for beneficial health effects.

Acknowledgements

This manuscript was developed as part of study conducted by Dr Joy Hussain during her PhD candidature at RMIT University.

Funding of this Study

Joy Hussain is supported by a PhD scholarship from the Jacka Foundation. No other sources of funding were involved.

References

1. M.L. Hannuksela and S. Ellahham. "Benefits and risks of sauna bathing," *The American journal of medicine*, vol. 110, no. 2, pp. 118-126, 2001.
2. R. Beever. "Far-infrared saunas for treatment of cardiovascular risk factors Summary of published evidence," *Canadian family physician*, vol. 55, no. 7, pp. 691-696, 2009.
3. T. Brockow, E. Conradi, G. Ebenbichler, A. Michalsen, and K.L. Resch. "The role of mild systemic heat and physical activity on endothelial function in patients with increased cardiovascular risk: results from a systematic review," *Forschende Komplementärmedizin/Research in Complementary Medicine*, vol. 18, no. 1, pp. 24-30, 2011.
4. M. Gayda, L. Bosquet, F. Paillard, et al. "Effects of sauna alone versus postexercise sauna baths on short-term heart rate variability in patients with untreated hypertension," *Journal of cardiopulmonary rehabilitation and prevention*, vol. 32, no. 3, pp. 147-154, 2012.
5. A.E. Littmann and R.K. Shields. "Whole body heat stress increases motor cortical excitability and skill acquisition in humans," *Clinical Neurophysiology*, vol. 127, no. 2, pp. 1521-1529, 2016.

6. G.M. Minnett, M. Skein, F. Bieuzen, et al. "Heat acclimation for protection from exertional heat stress," *The Cochrane Library*, 2016.
7. E.J. Calabrese and L.A. Baldwin. "Defining hormesis," *Human & experimental toxicology*, vol. 21, no. 2, pp. 91-97, 2002.
8. M.P. Mattson. "Hormesis defined," *Ageing research reviews*, vol. 7, no. 1, pp. 1-7, 2008.
9. R. Arena, M. Guazzi, L. Lianov, et al. "Healthy lifestyle interventions to combat noncommunicable disease—a novel nonhierarchical connectivity model for key stakeholders: a policy statement from the American Heart Association, European Society of Cardiology, European Association for Cardiovascular Prevention and Rehabilitation, and American College of Preventive Medicine," *European heart journal*, p. ehv207, 2015.
10. J. Tsonis. "Sauna Studies as an Academic Field: A New Agenda for International Research," *Literature & Aesthetics*, vol. 26, no. 1, 2017.
11. K. Kukkonen-Harjula, P. Oja, K. Laustiola, et al. "Haemodynamic and hormonal responses to heat exposure in a Finnish sauna bath," *European journal of applied physiology and occupational physiology*, vol. 58, no. 5, pp. 543-550, 1989.
12. W.J. Crinnion. "Sauna as a valuable clinical tool for cardiovascular, autoimmune, toxicant-induced and other chronic health problems," *Alternative Medicine Review*, vol. 16, no. 3, pp. 215-226, 2011.
13. J. Leppäluoto, P. Huttunen, J. Hirvonen, A. Väänänen, M. Tuominen, and J. Vuori. "Endocrine effects of repeated sauna bathing," *Acta Physiologica*, vol. 128, no. 3, pp. 467-470, 1986.
14. D. Jezova, Z. Radikova, and M. Vigas. "Growth hormone response to different consecutive stress stimuli in healthy men: Is there any difference?," *Stress*, vol. 10, no. 2, pp. 205-211, 2007.
15. T. Radtke, D. Poerschke, M. Wilhelm, et al. "Acute effects of Finnish sauna and cold-water immersion on haemodynamic variables and autonomic nervous system activity in patients with heart failure," *European journal of preventive cardiology*, vol. 23, no. 6, pp. 593-601, 2016.
16. C. Tomiyama, M. Watanabe, T. Honma, et al. "The effect of repetitive mild hyperthermia on body temperature, the autonomic nervous system, and innate and adaptive immunity," *Biomedical Research*, vol. 36, no. 2, pp. 135-142, 2015.
17. P. Zalewski, M. Zawadka-Kunikowska, J. Słomko, et al. "Cardiovascular and Thermal Response to Dry-Sauna Exposure in Healthy Subjects," *Physiology Journal*, vol. 2014, 2014.
18. Z.-D. Zhao, W.Z. Yang, C. Gao, et al. "A hypothalamic circuit that controls body temperature," *Proceedings of the National Academy of Sciences*, p. 201616255, 2017.
19. W.B. Liedtke. "Deconstructing mammalian thermoregulation," *Proceedings of the National Academy of Sciences*, p. 201620579, 2017.
20. M.J. Buono, S.L. Martha, and J.H. Heaney. "Peripheral sweat gland function, but not whole-body sweat rate, increases in women following humid heat acclimation," *Journal of thermal biology*, vol. 35, no. 3, pp. 134-137, 2010.
21. M. Zech, S. Bösel, M. Tuthorn, et al. "Sauna, sweat and science—quantifying the proportion of condensation water versus sweat using a stable water isotope (2H/1H and 18O/16O) tracer experiment," *Isotopes in environmental and health studies*, no. ahead-of-print, pp. 1-9, 2015.
22. M. Iguchi, A.E. Littmann, S.-H. Chang, L.A. Wester, J.S. Knipper, and R.K. Shields. "Heat stress and cardiovascular, hormonal, and heat shock proteins in humans," *Journal of athletic training*, vol. 47, no. 2, pp. 184-190, 2012.
23. F.F. Moghadam, M. Bakhshandeh, and H. Sahinbas. "A brief review of Hyperthermia as a neoadjuvant therapy method related to cancer treatment," *Journal of Cellular Immunotherapy*, vol. 3, no. 1, p. 8, 2017.
24. T. Mussivand, H. Alshaer, H. Haddad, et al. "Thermal therapy: a viable adjunct in the treatment of heart failure?," *Congestive Heart Failure*, vol. 14, no. 4, pp. 180-186, 2008.
25. M.A. Petrie, A.L. Kimball, C.L. McHenry, et al. "Distinct skeletal muscle gene regulation from active contraction, passive vibration, and whole body heat stress in humans," *PLoS one*, vol. 11, no. 8, p. e0160594, 2016.
26. J.C. Harvey, B.T. Roseguini, B.M. Goerger, E.A. Fallon, and B.J. Wong. "Acute Thermotherapy Prevents Impairments in Cutaneous Microvascular Function Induced by a High Fat Meal," *Journal of Diabetes Research*, vol. 2016, 2016.
27. A. Garolla, M. Torino, B. Sartini, et al. "Seminal and molecular evidence that sauna exposure affects human spermatogenesis," *Human Reproduction*, vol. 28, no. 4, pp. 877-885, 2013.
28. K. Kukkonen-Harjula and K. Kauppinen. "Health effects and risks of sauna bathing," *International Journal of Circumpolar Health*, vol. 65, no. 3, 2006.
29. N. Kluger. "Sauna: cardiac and vascular benefits and risks," *Presse medicale (Paris, France: 1983)*, vol. 40, no. 10, pp. 895-899, 2011.

30. S. Shui, X. Wang, J.Y. Chiang, and L. Zheng. "Far-infrared therapy for cardiovascular, autoimmune, and other chronic health problems: A systematic review," *Experimental Biology and Medicine*, vol. 240, no. 10, pp. 1257-1265, 2015.
31. D. Moher, A. Liberati, J. Tetzlaff, D.G. Altman, and P. Group. "Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement," *PLoS medicine*, vol. 6, no. 7, p. e1000097, 2009.
32. J.P. Higgins, D.G. Altman, P.C. Gøtzsche, et al. "The Cochrane Collaboration's tool for assessing risk of bias in randomised trials," *Bmj*, vol. 343, p. d5928, 2011.
33. A.R. Jadad, R.A. Moore, D. Carroll, et al. "Assessing the quality of reports of randomized clinical trials: is blinding necessary?," *Controlled clinical trials*, vol. 17, no. 1, pp. 1-12, 1996.
34. A. Masuda, T. Kihara, T. Fukudome, T. Shinsato, S. Minagoe, and C. Tei. "The effects of repeated thermal therapy for two patients with chronic fatigue syndrome," *Journal of psychosomatic research*, vol. 58, no. 4, pp. 383-387, 2005.
35. C. Tei, T. Imamura, K. Kinugawa, et al. "Waon Therapy for Managing Chronic Heart Failure—Results From a Multicenter Prospective Randomized WAON-CHF Study—," *Circulation Journal*, vol. 80, no. 4, pp. 827-834, 2016.
36. G. Kanji, M. Weatherall, R. Peter, G. Purdie, and R. Page. "Efficacy of regular sauna bathing for chronic tension-type headache: a randomized controlled study," *The Journal of Alternative and Complementary Medicine*, vol. 21, no. 2, pp. 103-109, 2015.
37. D. Pach, B. Knöchel, R. Lüdtke, K. Wruck, S.N. Willich, and C.M. Witt. "Visiting a sauna: does inhaling hot dry air reduce common cold symptoms? A randomised controlled trial," *Medical Journal of Australia*, vol. 193, no. 11, p. 730, 2010.
38. T. Laukkanen, H. Khan, F. Zaccardi, and J.A. Laukkanen. "Association between sauna bathing and fatal cardiovascular and all-cause mortality events," *JAMA internal medicine*, vol. 175, no. 4, pp. 542-548, 2015.
39. T. Laukkanen, S. Kunutsor, J. Kauhanen, and J.A. Laukkanen. "Sauna bathing is inversely associated with dementia and Alzheimer's disease in middle-aged Finnish men," *Age and Ageing*, 2016.
40. J. Stanley, A. Halliday, S. D'Auria, M. Buchheit, and A.S. Leicht. "Effect of sauna-based heat acclimation on plasma volume and heart rate variability," *European journal of applied physiology*, vol. 115, no. 4, pp. 785-794, 2015.
41. M. Hüppe, J. Müller, J. Schulze, H. Wernze, and P. Ohnsorge. "Treatment of patients burdened with lipophilic toxicants: A randomized controlled trial," *Acta Nerv Super Rediviva*, vol. 51, no. 3-4, pp. 133-141, 2009.
42. G.H. Ross and M.C. Sternquist. "Methamphetamine exposure and chronic illness in police officers significant improvement with sauna-based detoxification therapy," *Toxicology and industrial health*, vol. 28, no. 8, pp. 758-768, 2012.
43. K. AMANO, R. YANAGIHORI, and C. TEI. "Waon Therapy is Effective as the Treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome," *日本温泉気候物理医学会雑誌*, vol. 78, no. 3, pp. 285-302, 2015.
44. F.G. Oosterveld, J.J. Rasker, M. Floors, et al. "Infrared sauna in patients with rheumatoid arthritis and ankylosing spondylitis," *Clinical rheumatology*, vol. 28, no. 1, p. 29, 2009.
45. R. Beever. "The effects of repeated thermal therapy on quality of life in patients with type II diabetes mellitus," *The Journal of Alternative and Complementary Medicine*, vol. 16, no. 6, pp. 677-681, 2010.
46. Y. Soejima, T. Munemoto, A. Masuda, Y. Uwatoko, M. Miyata, and C. Tei. "Effects of Waon therapy on chronic fatigue syndrome: a pilot study," *Internal Medicine*, vol. 54, no. 3, pp. 333-338, 2015.
47. A. Masuda, Y. Koga, M. Hattanmaru, S. Minagoe, and C. Tei. "The effects of repeated thermal therapy for patients with chronic pain," *Psychotherapy and psychosomatics*, vol. 74, no. 5, pp. 288-294, 2005.
48. T. Otori, T. Nozawa, H. Ithori, et al. "Effect of repeated sauna treatment on exercise tolerance and endothelial function in patients with chronic heart failure," *The American journal of cardiology*, vol. 109, no. 1, pp. 100-104, 2012.
49. S. Fujita, Y. Ikeda, M. Miyata, et al. "Effect of Waon therapy on oxidative stress in chronic heart failure," *Circulation Journal*, vol. 75, no. 2, pp. 348-356, 2011.
50. S. Kuwahata, M. Miyata, S. Fujita, et al. "Improvement of autonomic nervous activity by Waon therapy in patients with chronic heart failure," *Journal of cardiology*, vol. 57, no. 1, pp. 100-106, 2011.
51. M. Miyata, T. Kihara, T. Kubozono, et al. "Beneficial effects of Waon therapy on patients with chronic heart failure: results of a prospective multicenter study," *Journal of cardiology*, vol. 52, no. 2, pp. 79-85, 2008.
52. H. Miyamoto, H. Kai, H. Nakaura, et al. "Safety and efficacy of repeated sauna bathing in patients with chronic systolic heart failure: a preliminary report," *Journal of cardiac failure*, vol. 11, no. 6, pp. 432-436, 2005.
53. T. Kihara, S. Biro, Y. Ikeda, et al. "Effects of repeated sauna treatment on ventricular arrhythmias in patients with chronic heart failure," *Circulation Journal*, vol. 68, no. 12, pp. 1146-1151, 2004.
54. Y. Sugahara, M. Ishii, H. Muta, K. Egami, T. Akagi, and T. Matsuishi. "Efficacy and safety of thermal vasodilation therapy by sauna in infants with severe congestive heart failure secondary to ventricular septal defect," *The American journal of cardiology*, vol. 92, no. 1, pp. 109-113, 2003.

55. T. Kihara, S. Biro, M. Imamura, et al. "Repeated sauna treatment improves vascular endothelial and cardiac function in patients with chronic heart failure," *Journal of the American College of Cardiology*, vol. 39, no. 5, pp. 754-759, 2002.
56. A. Masuda, M. Miyata, T. Kihara, S. Minagoe, and C. Tei. "Repeated Sauna Therapy Reduces Urinary 8-Epi-Prostaglandin F2. ALPHA," *Japanese heart journal*, vol. 45, no. 2, pp. 297-303, 2004.
57. S. Biro, A. Masuda, T. Kihara, and C. Tei. "Clinical implications of thermal therapy in lifestyle-related diseases," *Experimental Biology and Medicine*, vol. 228, no. 10, pp. 1245-1249, 2003.
58. M. Imamura, S. Biro, T. Kihara, et al. "Repeated thermal therapy improves impaired vascular endothelial function in patients with coronary risk factors," *Journal of the American College of Cardiology*, vol. 38, no. 4, pp. 1083-1088, 2001.
59. D. Gryka, W. Pilch, M. Szarek, Z. Szygula, and Ł. Tota. "The effect of sauna bathing on lipid profile in young, physically active, male subjects," *International journal of occupational medicine and environmental health*, vol. 27, no. 4, pp. 608-618, 2014.
60. W. Pilch, Z. Szygula, A. Klimek, et al. "Changes in the lipid profile of blood serum in women taking sauna baths of various duration," *International journal of occupational medicine and environmental health*, vol. 23, no. 2, pp. 167-174, 2010.
61. Z. Szygula, A. Tyka, T.P. DG, G. Lech, T. Cison, and B. Kita. "EFFECT OF 30-MINUTE SAUNA SESSIONS ON LIPID PROFILE IN YOUNG WOMEN," *Med Sport*, vol. 18, no. 4, pp. 165-171, 2014.
62. T. Shinsato, M. Miyata, T. Kubozono, et al. "Waon therapy mobilizes CD34+ cells and improves peripheral arterial disease," *Journal of cardiology*, vol. 56, no. 3, pp. 361-366, 2010.
63. C. Tei, T. Shinsato, M. Miyata, T. Kihara, and S. Hamasaki. "Waon Therapy Improves Peripheral Arterial Disease," *Journal of the American College of Cardiology*, vol. 50, no. 22, p. 2169, 2007.
64. H. Kikuchi, N. Shiozawa, S. Takata, K. Ashida, and F. Mitsunobu. "Effect of repeated Waon therapy on exercise tolerance and pulmonary function in patients with chronic obstructive pulmonary disease: a pilot controlled clinical trial," *International journal of chronic obstructive pulmonary disease*, vol. 9, p. 9, 2014.
65. M. Umehara, A. Yamaguchi, S. Itakura, et al. "Repeated Waon therapy improves pulmonary hypertension during exercise in patients with severe chronic obstructive pulmonary disease," *Journal of cardiology*, vol. 51, no. 2, pp. 106-113, 2008.
66. T. Kihara, M. Miyata, T. Fukudome, et al. "Waon therapy improves the prognosis of patients with chronic heart failure," *Journal of cardiology*, vol. 53, no. 2, pp. 214-218, 2009.
67. M. Sobajima, T. Nozawa, H. Ihori, et al. "Repeated sauna therapy improves myocardial perfusion in patients with chronically occluded coronary artery-related ischemia," *International journal of cardiology*, vol. 167, no. 1, pp. 237-243, 2013.
68. S. Matsumoto, M. Shimodozono, S. Etoh, R. Miyata, and K. Kawahira. "Effects of thermal therapy combining sauna therapy and underwater exercise in patients with fibromyalgia," *Complementary therapies in clinical practice*, vol. 17, no. 3, pp. 162-166, 2011.
69. A. Masuda, M. Nakazato, T. Kihara, S. Minagoe, and C. Tei. "Repeated thermal therapy diminishes appetite loss and subjective complaints in mildly depressed patients," *Psychosomatic medicine*, vol. 67, no. 4, pp. 643-647, 2005.
70. N. Kunbootsri, T. Janyacharoen, P. Arrayawichanon, et al. "The effect of six-weeks of sauna on treatment autonomic nervous system, peak nasal inspiratory flow and lung functions of allergic rhinitis Thai patients," *Asian Pacific Journal of Allergy and Immunology*, vol. 31, no. 2, p. 142, 2013.
71. V. Zinchuk and D. Zhadzko. "Sauna effect on blood oxygen transport and prooxidant-antioxidant balance in athletes," *Medicina Sportiva: Journal of Romanian Sports Medicine Society*, vol. 8, no. 3, p. 1883, 2012.
72. W. Pilch, Z. Szygula, and M. Torii. "Effect of the sauna-induced thermal stimuli of various intensity on the thermal and hormonal metabolism in women," *Biology of Sport*, vol. 24, no. 4, p. 357, 2007.
73. D. Kowatzki, C. Macholdt, K. Krull, et al. "Effect of regular sauna on epidermal barrier function and stratum corneum water-holding capacity in vivo in humans: a controlled study," *Dermatology*, vol. 217, no. 2, pp. 173-180, 2008.
74. C. Tei. "Waon therapy: soothing warmth therapy," *J Cardiol*, vol. 49, no. 6, pp. 301-304, 2007.
75. O. Luurila, "Cardiac arrhythmias, sudden death and the Finnish sauna bath," in *Sudden Coronary Death*, pp. 73-81: Karger Publishers: 1978.
76. O.J. Luurila. "The sauna and the heart," *Journal of internal medicine*, vol. 231, no. 4, pp. 319-320, 1978.
77. K. Kukkonen-Harjula, P. Oja, I. Vuori, et al. "Cardiovascular effects of atenolol, scopolamine and their combination on healthy men in Finnish sauna baths," *European journal of applied physiology and occupational physiology*, vol. 69, no. 1, pp. 10-15, 1994.

78. M.L. Keast and K.B. Adamo. "The Finnish sauna bath and its use in patients with cardiovascular disease," *Journal of cardiopulmonary rehabilitation and prevention*, vol. 20, no. 4, pp. 225-230, 2000.
79. J.R. Basford, J.K. Oh, T.G. Allison, et al. "Safety, acceptance, and physiologic effects of sauna bathing in people with chronic heart failure: a pilot report," *Archives of physical medicine and rehabilitation*, vol. 90, no. 1, pp. 173-177, 2009.
80. M. Kivimäki, M. Virtanen, and J.E. Ferrie. "The Link Between Sauna Bathing and Mortality May Be Noncausal," *JAMA internal medicine*, vol. 175, no. 10, pp. 1718-1718, 2015.
81. A.A. Miragem and P.I. Homem de Bittencourt. "Nitric oxide-heat shock protein axis in menopausal hot flashes: neglected metabolic issues of chronic inflammatory diseases associated with deranged heat shock response," *Human Reproduction Update*, pp. 1-29, 2017.
82. A.S. Leon and O.A. Sanchez. "Response of blood lipids to exercise training alone or combined with dietary intervention," *Medicine & Science in Sports & Exercise*, vol. 33, no. 6, pp. S502-S515, 2001.
83. S.J. Genuis, M.E. Sears, G. Schwalfenberg, J. Hope, and R. Bernhoft. "Clinical detoxification: elimination of persistent toxicants from the human body," *The Scientific World Journal*, vol. 2013, 2013.
84. M.E. Sears, K.J. Kerr, and R.I. Bray. "Arsenic, cadmium, lead, and mercury in sweat: a systematic review," *Journal of environmental and public health*, vol. 2012, 2012.
85. S.K. Genuis, D. Birkholz, and S.J. Genuis. "Human Excretion of Polybrominated Diphenyl Ether Flame Retardants: Blood, Urine, and Sweat Study," *Biomed Res Int*, vol. 2017, p. 3676089, 2017.
86. S.J. Genuis, K. Lane, and D. Birkholz. "Human Elimination of Organochlorine Pesticides: Blood, Urine, and Sweat Study," *Biomed Res Int*, vol. 2016, p. 1624643, 2016.
87. S.J. Genuis, S. Beeson, D. Birkholz, and R.A. Lobo. "Human excretion of bisphenol A: blood, urine, and sweat (BUS) study," *Journal of environmental and public health*, vol. 2012, 2012.
88. S.J. Genuis, S. Beeson, R.A. Lobo, and D. Birkholz. "Human elimination of phthalate compounds: blood, urine, and sweat (BUS) study," *The Scientific World Journal*, vol. 2012, 2012.
89. E.J. Cone, M.J. Hills Grove, A.J. Jenkins, R.M. Keenan, and W.D. Darwin. "Sweat testing for heroin, cocaine, and metabolites," *Journal of Analytical Toxicology*, vol. 18, no. 6, pp. 298-305, 1994.
90. N. De Giovanni and N. Fucci. "The current status of sweat testing for drugs of abuse: a review," *Current medicinal chemistry*, vol. 20, no. 4, pp. 545-561, 2013.
91. J.N. Hussain, N. Mantri, and M.M. Cohen. "Working Up a Good Sweat—The Challenges of Standardising Sweat Collection for Metabolomics Analysis," *Clin Biochem Rev*, vol. 38, no. 1, p. 13, 2017.
92. R. Przewlocki, "Opioid Peptides," in *Neuroscience in the 21st Century*, pp. 1525-1553: Springer: 2013.
93. V. Koljonen. "Hot air sauna burns—review of their etiology and treatment," *Journal of burn care & research*, vol. 30, no. 4, pp. 705-710, 2009.
94. N. Giannetti, M. Juneau, A. Arsenault, et al. "Sauna-induced myocardial ischemia in patients with coronary artery disease," *The American journal of medicine*, vol. 107, no. 3, pp. 228-233, 1999.
95. G.G.R. Sforza and A. Marinou. "Hypersensitivity pneumonitis: a complex lung disease," *Clinical and Molecular Allergy*, vol. 15, no. 1, p. 6, 2017.
96. K.J. Chen, T.H. Chen, Y.M. Sue, T.J. Chen, and C.Y. Cheng. "High-volume plasma exchange in a patient with acute liver failure due to non-exertional heat stroke in a sauna," *Journal of clinical apheresis*, vol. 29, no. 5, pp. 281-283, 2014.
97. T. Wessapan and P. Rattanadecho. "Heat transfer analysis of the human eye during exposure to sauna therapy," *Numerical Heat Transfer, Part A: Applications*, vol. 68, no. 5, pp. 566-582, 2015.
98. J.G. Heckmann, C. Rauch, S. Seidler, M. Dütsch, and B. Kasper. "Sauna stroke syndrome," *Journal of Stroke and Cerebrovascular Diseases*, vol. 14, no. 3, pp. 138-139, 2005.
99. A. Kenttämies and K. Karkola. "Death in sauna," *Journal of forensic sciences*, vol. 53, no. 3, pp. 724-729, 2008.
100. A. Rodhe and A. Eriksson. "Sauna deaths in Sweden, 1992–2003," *The American journal of forensic medicine and pathology*, vol. 29, no. 1, pp. 27-31, 2008.
101. A. Jung and H.C. Schuppe. "Influence of genital heat stress on semen quality in humans," *Andrologia*, vol. 39, no. 6, pp. 203-215, 2007.
102. H. Guo, H. Zhang, B. Xue, Y. Sha, Y. Liu, and R. Liu. "Effects of cigarette, alcohol consumption and sauna on sperm morphology," *Zhonghua nan ke xue= National journal of andrology*, vol. 12, no. 3, pp. 215-217, 221, 2006.
103. J. Saikhun, Y. Kitiyanant, V. Vanadurongwan, and K. Pavasuthipaisit. "Effects of sauna on sperm movement characteristics of normal men measured by computer-assisted sperm analysis," *International journal of andrology*, vol. 21, no. 6, pp. 358-362, 1998.
104. P. Brown-Woodman, E. Post, G. Gass, and I. White. "The effect of a single sauna exposure on spermatozoa," *Archives of andrology*, vol. 12, no. 1, pp. 9-15, 1984.
105. M. Sarner. "Inconceivable truth," *New Scientist*, vol. 236, no. 3152, pp. 28-32, 2017.

106. S.K. Kunutsor, T. Laukkanen, and J.A. Laukkanen. "Sauna bathing reduces the risk of respiratory diseases: a long-term prospective cohort study," *European journal of epidemiology*, pp. 1-5, 2017.
107. S.K. Kunutsor, T. Laukkanen, and J.A. Laukkanen. "Frequent sauna bathing may reduce the risk of pneumonia in middle-aged Caucasian men: The KIH prospective cohort study," *Respiratory medicine*, vol. 132, pp. 161-163, 2017.
108. J.A. Laukkanen and T. Laukkanen. "Sauna bathing and systemic inflammation," *European journal of epidemiology*, pp. 1-3, 2017.
109. F. Zaccardi, T. Laukkanen, P. Willeit, S.K. Kunutsor, J. Kauhanen, and J.A. Laukkanen. "Sauna Bathing and Incident Hypertension: A Prospective Cohort Study," *American Journal of Hypertension*, 2017.
110. S.K. Kunutsor, H. Khan, T. Laukkanen, and J.A. Laukkanen. "Joint associations of sauna bathing and cardiorespiratory fitness on cardiovascular and all-cause mortality risk: a long-term prospective cohort study," *Annals of medicine*, pp. 1-8, 2017.