THE EFFECTS OF HIGH-INTENSITY INTERVAL TRAINING ON PAIN PARAMETERS AND SLEEP QUALITY IN OVERWEIGHT AND HEALTHY-WEIGHT WOMEN

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Declaration

I, Zianca Smit, declare that this Dissertation is my own, unaided work. It is being submitted for the degree of Master of Science at the University of the Witwatersrand, Johannesburg. It has not been submitted for any degree or examination at any other University.

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Signature of candidate

Abstract

The relationship between overweight, pain and poor sleep quality is a complex network of cause and effect, potentially mediated by central adiposity. Exercise, more specifically high-intensity interval training (HIIT), may reduce pain and improve poor sleep quality. However, limited research on the effects of HIIT on pain and sleep quality is available, especially in an overweight, female population. The dissertation assessed the efficacy of a 14-week HIIT intervention for reducing pain and improving sleep quality in overweight and healthy weight women.

Overweight (n=21) and healthy-weight (n=17) women were grouped into exercising (overweight n = 10, healthy-weight n = 10) and non-exercising groups (overweight n = 11, healthy-weight n = 7). Exercising groups participated in a 14-week home-based, dynamic resistance HIIT intervention, whereas non-exercising groups maintained habitual sedentary activity. Anthropometry, pain perception (cold-, heat-, mechanical-, pressure pain thresholds, ischaemic pain rating) and sleep quality (Pittsburgh sleep quality index; PSQI) were assessed before and after the 14-week intervention.

The 14-week HIIT intervention reduced waist circumference of the overweight women (baseline = 112.9 (21.7) cm; post-intervention = 101.3 (18.6) cm; p<0.001), but did not alter body mass, body fat percentage, hip circumference, waist-to-hip ratio or VO_{2peak} in either the healthy-weight or the overweight women. Post-intervention cold pain sensitivity was increased in the exercising (baseline = 6.9 [5.2-9.9] °C; post-intervention = 12.3 [10.0-25.1] °C; p<0.05) and non-exercising (baseline = 8.1 [5.5-12.3] °C; post-intervention = 17.6 [10.7-20.9] °C; p<0.05) overweight women. Baseline sleep quality was poor in the overweight women according to PSQI global scores (baseline PSQI; overweight exercising group = 8.0 (1.9), overweight non-exercising group = 4.9 (3.3)). The sleep quality component score of the PSQI was improved in the exercising overweight women (baseline = 1.8 (0.8); post-intervention = 0.8 (0.4); p<0.05). Post-intervention pain perception and sleep quality of healthy-weight women remained unaltered. Associations were observed between the following variables: decreased heat pain sensitivity and increased body mass index (r=0.301, p=0.042); increased waist circumference and both poor sleep quality (r_s=0.325, p=0.049) and reduced sleep duration (r_s=0.488, p=0.005) assessed at baseline in the combined study sample.

The current dissertation demonstrates that HIIT may be a time-efficient intervention for improving sleep quality in overweight women with poor sleep quality. Moreover, the results support the notion that exercise may increase pain sensitivity in an overweight population. Additionally, this study shows that increased BMI may mediate increased pain perception while increased waist circumference may mediate poor sleep quality in South African women.

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Abbreviations

AUC	Area under the curve
BMI	Body mass index
EIH	Exercise-induced hypoalgesia
H-HIIT	Exercising healthy weight participants
HIIT	High-intensity interval training
H-nonHIIT	Non-exercising healthy weight participants
HR_{max}	Maximum heart rate
Lep-R	Leptin receptor
MICT	Moderate-intensity continuous training
NNT	Number needed to treat
O-HIIT	Exercising overweight participants
O-nonHIIT	Non-exercising overweight participants
PSG	Polysomnography
PSQI	Pittsburgh Sleep Quality Index
QST	Quantitative sensory test
REM	Rapid eye movement (sleep stage)
RPE	Rate of perceived exertion
VAS	Visual analogue scale
VO_{2peak}	Peak oxygen consumption

1. INTRODUCTION

The World Health Organisation reported four million annual deaths attributable to overweight and obesity in 2017 (WHO, 2017). Obesity and overweight are associated with reduced quality of life and impaired functional mobility (Guh *et al.*, 2009), usually attributed to common comorbidities associated with obesity and overweight, including chronic pain (Wright *et al.*, 2010) and poor sleep quality (Vargas *et al.*, 2014). More than half of the South African female population (60%) is either overweight or obese (body mass index (BMI) $\geq$ 25 kg/m^2) (Shisana *et al.*, 2013). Moreover, chronic pain conditions (19.9%) and poor sleep quality (31.3%) are prevalent in South African women (Stranges *et al.*, 2012; Shisana *et al.*, 2013). Added to this prevalence, pain and poor sleep quality have a reciprocal and perpetual relationship, such that pain disrupts sleep and poor sleep exacerbates pain (Finan *et al.*, 2013).

Patients commonly seek treatment for chronic pain and/or poor sleep quality (Shisana *et al.*, 2013). The most common therapeutic treatments used to manage chronic pain and poor sleep quality are various pharmacological agents, including oxycodone and benzodiazepines (Thomazeau *et al.*, 2014; Kripke, 2016), respectively. These pharmacological agents are costly and associated with poor efficacy and adverse side effects, including drug dependency and daytime dysfunction (Bloomquist, 1963; Kripke, 2016). Hence the need to incorporate non-pharmacological interventions for the improvement of chronic pain and poor sleep quality which may reduce the use of pharmacological agents as well as the adverse side effects associated with them. Exercise may be an inexpensive, non-pharmacological therapeutic treatment to manage pain (Rice *et al.*, 2019) and poor sleep quality (Driver & Taylor, 2000) associated with obesity.

In this section of my dissertation, I will briefly discuss the literature pertaining to the relationship between obesity and both pain and poor sleep quality. Thereafter, I will critically review the literature assessing the effects of exercise on both pain perception and poor sleep quality in healthy-weight, overweight and obese individuals. Lastly, I will discuss the rationale, including the aim, objectives and hypothesis, for my dissertation.

1.1 The Relationship of Overweight and Obesity with Pain and Sleep Quality

The relationship of BMI with pain and sleep quality consist of a complex network of multidimensional interactions (Figure 1.1). For instance, overweight (BMI $\geq$ 25 kg/m^2) and

obesity (BMI ≥ 30 kg/m^2) are associated with chronic pain (Mork *et al.*, 2013) and poor sleep quality (Ogretmenoglu *et al.*, 2005). Also, poor sleep quality is associated with an increased risk of obesity (Gangwisch *et al.*, 2005) and an augmentation of pain sensitivity (Lautenbacher *et al.*, 2006), while increased pain results in poor sleep quality (Moldofsky, 2001).

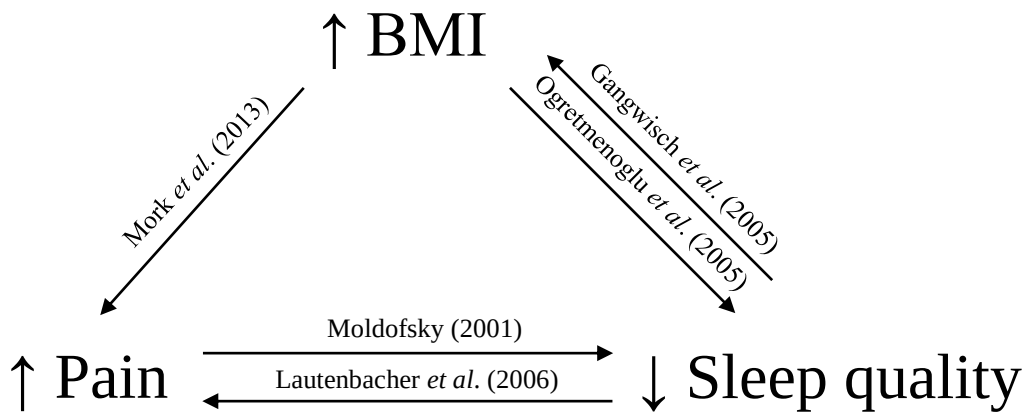


Figure 1.1: The complex relationship between sleep quality, body mass index (BMI) and pain. ↑: increased, ↓: decreased

1.1.1 The relationship of overweight and obesity with pain

Obesity and chronic pain conditions commonly co-exist (Torensma *et al.*, 2016). According to the International Association for the Study of Pain (IASP), pain is defined as "an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage" (Raja *et al.*, 2020, p. 2). Once pain persists more than three months, it is referred to as chronic pain (IASP, 2019). Although obesity and chronic pain conditions are commonly associated in epidemiological studies (Hitt *et al.*, 2007; Wright *et al.*, 2010; Stone & Broderick, 2012), the exact mechanism for the association is not well defined. Assessing experimental pain models, whereby pain is induced experimentally in participants, gives an insight into the nociceptive transmission in the central nervous system of overweight and obese individuals. Understanding how experimental pain is perceived in an overweight and obese population, compared to healthy-weight controls, may aid in the understanding of the underlying

pathology mediating obesity-related chronic pain. Ultimately, with greater understanding, appropriate interventions may be implemented to improve obesity-related chronic pain. A summary of studies that have assessed experimental pain models in obese versus healthy-weight participants is seen in Table 1.1.

Table 1.1: Studies assessing experimentally-induced pain perception in obese versus healthy-weight participants

Reference	n (% obese)	Pain perception assessed	Site of pain stimulus	Pain perception compared to healthy weight controls
McKendall & Haier (1983)	60 (43%)	Pressure pain threshold and pressure pain tolerance	Index finger	Decreased pain threshold and pain tolerance
Zahorska-Markiewicz *et al.* (1983)	40 (50%)	Electrical pain threshold	Forearm	Increased pain threshold
Miscio *et al.* (2005)	41 (51%)	Cold pain threshold	Index finger, little finger and big toe	Index: Increased pain threshold Little: Increased pain threshold Toe: No difference
	41 (51%)	Heat pain threshold	Index finger, little finger and big toe	Index: Increased Little: Increased Toe: No difference
Price *et al.* (2013)	20 (50%)	Cold pain threshold and cold pain rating	Forehead and abdomen	Forehead: No difference Abdomen: Increased pain threshold
	20 (50%)	Heat pain threshold and heat pain tolerance	Forehead and abdomen	Forehead: No difference Abdomen: Increased pain threshold and tolerance
	20 (50%)	Pressure pain threshold	Hand	No difference

The evaluation of experimental pain models using pain thresholds ("minimum intensity of a stimulus that is perceived as painful"; IASP, 2017), pain tolerance ("maximum intensity of a

pain-producing stimulus that a subject is willing to accept"; IASP 2017) and/or pain ratings on a visual scale (0-100 mm line anchored from "no pain" to "worst pain ever") in obese participants, compared to healthy-weight controls have yielded equivocal results (Table 1.1). Some studies reported no differences in pain sensitivity between healthy-weight and obese individuals (Miscio *et al.*, 2005; Price *et al.*, 2013),while others have shown that obese individuals have increased (Zahorska-Markiewicz *et al.*, 1983; Miscio *et al.*, 2005; Price *et al.*, 2013), or decreased (McKendall & Haier, 1983) pain thresholds and pain tolerances compared to healthy-weight controls.

Conflicting results may be attributed to the different sites at which pain was assessed (Price *et al.*, 2013). More specifically, in anatomical areas with excess adipose tissue in obese individuals, such as the abdomen and arm, pain thresholds and pain tolerances are increased, suggesting reduced pain sensitivity, compared to healthy-weight controls (Zahorska-Markiewicz *et al.*, 1983; Price *et al.*, 2013). Whilst, in areas of similar adiposity, such as the forehead, pain perception is comparable between obese and healthy-weight participants (Price *et al.*, 2013). As such, it has been hypothesised that excess adipose tissue impedes pain transmission, and hence, reduces pain sensitivity (Price *et al.*, 2013). However, some authors do not support this hypothesis, as some studies have shown that obese participants have increased (Miscio *et al.*, 2005) or decreased (McKendall & Haier, 1983) pain thresholds in areas of similar adipose tissue, compared to healthy-weight controls. Thus, factors other than volume of adipose tissue are attributable to the conflicting pain results summarised in Table 1.1.

The release of cytokines from excess adipose tissue, rather than the hinderance of pain transmission by excess tissue, may offer some explanation to the conflicting pain results (Zhang & An, 2007). Excess adipose tissue is associated with the increased release of proinflammatory cytokines, such as leptin (Maury *et al.*, 2007). Leptin, the hormone primarily associated with satiety, also inhibits the descending *inhibitory* pain pathway (Cristino *et al.*, 2016); therefore, increasing the perception of pain due to decreased inhibition. As such, one would expect an increased pain perception in areas of excess adipose tissue and, if circulated systemically, an increased pain perception throughout the body. However, the prolonged release of leptin may cause leptin receptor (Lep-R) desensitisation (Cristino *et al.*, 2016), which, in theory, should reduce such increased sensitivity to pain. Lep-R desensitisation may, in fact, result in increased

activity of the inhibitory pain pathway; and therefore, reduced pain perception (Cristino *et al.*, 2016).

Others report no change, or increased pain sensitivity (decreased pain threshold/tolerance) in obese individuals in areas with no or low adipose tissue, such as the forehead and fingertips, compared to healthy-weight controls (McKendall & Haier, 1983; Miscio *et al.*, 2005; Price *et al.*, 2013). Perhaps the Lep-R desensitisation, and hence reduced pain perception, may only occur in areas of excess adipose tissue, such as the abdomen, from which increased leptin is released. Furthermore, hypothetically, if the increased release of leptin from adipose tissue is spread systemically, areas with no or low adipose tissue will have no change or increased pain sensitivity due to no Lep-R desensitisation in these areas. In support of this theory, studies that have assessed pain in both areas of excess adipose tissue, such as the abdomen, and areas with little to no adipose tissue, such as the forehead, have found reduced pain sensitivity in the abdomen with no change in the forehead in obese individuals, compared with healthy-weight controls (Price *et al.*, 2013). Additionally, further supporting the Lep-R desensitisation theory, is the fact that leptin resistance (the inability of leptin to limit energy intake) is well documented in obese individuals (Enriori *et al.*, 2006).

In contrast to the Lep-R desensitisation theory, Miscio *et al.* (2005) reported increased thermal (heat and cold) pain thresholds, and hence reduced thermal-pain sensitivity, in obese participants, compared to healthy-weight controls, measured in an area of low adipose tissue, such as the finger tips. The authors suggested that differences in pain perception, especially in thermal pain, may be an indication of early peripheral neuropathy as a result of hyperinsulinemia associated with obesity (Miscio *et al.*, 2005). Thus, impaired insulin metabolism may interrupt the transmission of action potentials through the nerve membrane, impairing sensory function (Brismar *et al.*, 1987; Brismar, 1993).

In summary, obesity-induced systemic inflammation and the increased release of leptin from adipose tissue may influence pain perception in the obese population. However, it is unclear whether subcutaneous or visceral (central) obesity is the main contributor to the altered pain perception observed in obese individuals. Therefore, future studies should assess the association between pain perception and both subcutaneous and visceral adiposity. Nevertheless, it is hypothesised that visceral adiposity (central obesity) mediates altered pain seen in an obese

population (Ray *et al.*, 2011), as visceral adiposity is the main source of inflammatory cytokines and leptin (Maury *et al.*, 2007).

Not only are data limited on differences in pain perception between obese and healthy-weight individuals, but also, there are limited data on whether *overweight* participants (BMI between 25 and 29 kg/m^2) perceive pain differently compared to healthy-weight controls. According to an extensive literature review, only one study has assessed the pain perception in overweight participants compared with healthy-weight controls (Tashani *et al.*, 2017). No differences in pain perception (heat pain threshold, cold pain threshold, pressure pain threshold, heat pain tolerance, cold pain tolerance and cold pain rating) is reported between overweight and healthy-weight women measured in different anatomical areas (dorsal thumb web, suprailiac, hand) (Tashani *et al.*, 2017). Therefore, the mechanisms responsible for mediating the difference in pain perception between obese participants and healthy-weight controls, such as central obesity, may not be present in overweight participants. However, more research is required to determine whether overweight participants perceive pain similarly compared with healthy-weight controls. Understanding how experimental pain is perceived by healthy-weight, overweight and obese participants may also underpin why some interventions, such as topical capsaicin, do not improve or even exacerbate (Mason *et al.*, 2004) chronic pain disorders common amongst overweight or obese individuals, such as neuropathy and musculoskeletal disorders.

1.1.2 The relationship of overweight and obesity with sleep quality

Sleep acts to restore homeostasis by regulating most, if not all, physiological and psychological behaviours (Rechtschaffen & Siegel, 2000). Neural networks contributing to the generation of sleep/wake states and the circadian mechanisms that control their timing have previously been described using animal and human models (Scammell *et al.*, 2017). In summary, monoaminergic neurons arising from various brain regions, including the locus coeruleus, tuberomammillary nucleus and the parabrachial nucleus, innervate the basal forebrain, cortex, thalamus and hypothalamus to promote wakefulness (Saper *et al.*, 2005; Fuller *et al.*, 2006). Neurons, such as GABAergic cortical interneurons, release nitric oxide synthase that promote sleep through mechanisms that are not fully understood (Morairty *et al.*, 2013).

Good sleep quality is paramount for a good quality of life and overall health (Strine & Chapman, 2005). Buysse (2014, p. 12) defines good sleep quality according to the following parameters "subjective satisfaction, appropriate timing, adequate duration, high efficiency and sustained alertness during waking hours". Although the complete understanding of sleep regulation and sleep function remain elusive, differences in sleep regulation and sleep quality amongst healthy-weight, overweight and obese populations can be assessed objectively and subjectively. The gold-standard to measure sleep objectively is polysomnography (PSG), where recordings from the electroencephalogram (brain activity), the electro-oculogram (eye movement) and the electromyogram (muscle activity) are used collectively as biomarkers of sleep/wake states, and to identify the various stages of sleep (Carskadon & Dement, 2011). Other objective techniques used to measure sleep include actigraphy whereby participants wear an accelerometer on their hip or non-dominant wrist. Although PSG recordings provide the most accurate measure of sleep, actigraphy offers a practical, less expensive and less invasive, objective measure of sleep (Buysse, 2014). Subjective measures of sleep include the use of questionnaires, such as the widely-used and validated Pittsburgh Sleep Quality Index (PSQI) (Buysse *et al.*, 1989); visual analogue scales (VAS) in which sleep parameters, such as subjective sleep quality and morning vigilance are self-rated on a 100 mm scale; and sleep diaries in which sleep parameters, such as sleep- and wake times and sleep duration, are self-recorded. Overall, subjective techniques tend to compliment objective techniques in adults (Buysse, 2014).

Cross-sectional studies have shown that obesity is associated with poor sleep quality assessed objectively (Theorell-Haglöw *et al.*, 2010; Moraes *et al.*, 2013) and subjectively (Anic *et al.*, 2010; Ford *et al.*, 2014; Vargas *et al.*, 2014; Furuncuoğlu *et al.*, 2016). Some show that central obesity, specifically in the form of waist circumference and saggital abdominal diameter, rather than BMI, is more strongly associated with poor sleep quality (Grunstein *et al.*, 1993; Davidson & Patel, 2008; Theorell-Haglöw *et al.*, 2010; Ford *et al.*, 2014). Moreover, longitudinal studies have shown that poor sleep quality, in the form of reduced sleep durations (≤ 5 hours), is a significant predictor of increased BMI and fat accumulation over five to six years from baseline (Chaput *et al.*, 2008; Hairston *et al.*, 2010). It has been suggested that reduced sleep durations, associated with reduced leptin concentrations, and thereby the feeling of hunger (Spiegel *et al.*,

2004), may increase caloric intake leading to weight gain and fat accumulation (Patel & Hu, 2008).

The reciprocal relationship, whereby obesity results in poor sleep quality, has also been described (Muscogiuri *et al.*, 2019). A common mechanism for obesity-induced sleep impairments, such as sleep-disordered breathing, relates to excess weight and increased pressure on the respiratory pathways of obese individuals, causing the diameter of the upper respiratory airways to either reduce or collapse (Isono, 2012). Reductions in respiratory diameters and, or frequent respiratory collapses may result in sleep disordered breathing, such as obstructive sleep apnoea (Gami *et al.*, 2003). Sleep disordered breathing reduces oxygen saturation of the blood (≥ 4%) and, consequently, arousals during sleep (Fleetham *et al.*, 2006), disrupting sleep architecture and sleep quality. An additional theory suggests that a high-fat and high-sugar diet may disrupt sleep quality (Grandner *et al.*, 2010; St-Onge *et al.*, 2016). More specifically, one study showed that objectively-measured slow wave sleep (deep sleep) was reduced and nocturnal arousals increased after a day of high saturated fat and high-sugar diet, compared to a four-day controlled diet in 26 healthy adults (St-Onge *et al.*, 2016). Also, high fat diets were negatively correlated with objectively-measured sleep durations in 459 postmenopausal women over a three-month period (Grandner *et al.*, 2010). Because sleep acts to restore energy (Rechtschaffen & Siegel, 2000; Siegel, 2005), it has been hypothesised that a high-fat (high-energy) diet, as seen in an obese population (Lissner & Heitmann, 1995), may supplement an integral function of sleep; consequently reducing sleep duration (Grandner *et al.*, 2010).

As opposed to obesity, the association between poor sleep quality and overweight is understudied. To our knowledge, only one study has assessed the cross-sectional relationship between overweight and poor sleep quality (Hung *et al.*, 2013). In 2803 pain-free participants, poor sleep quality, specifically short sleep durations assessed by the PSQI, was found to be associated with overweight and obesity, especially in women (Hung *et al.*, 2013). No longitudinal study, to our knowledge, has assessed the relationship between overweight and poor sleep quality. Therefore, it is unknown whether poor sleep quality may precede becoming overweight, as seen with central obesity - where poor sleep quality is a predictor of increased BMI and fat accumulation. Consequently, more research, especially longitudinal analyses, on the

association between being overweight and poor sleep quality is required to identify the main contributor in the reciprocal relationship between BMI and sleep quality.

Understanding how poor sleep quality is related to overweight and obesity is important; particularly, since obesity and poor sleep quality have reciprocal relationships (i.e. poor sleep quality increases the risk of obesity and obesity leads to poor sleep quality (Gangwisch *et al.*, 2005; Ogretmenoglu *et al.*, 2005)).

1.2 Exercise as an Intervention to Improve Pain and Sleep Quality

Studies assessing the ability of exercise to improve pain and sleep quality have used acute (< one week) and regular (≥ one week (Kredlow *et al.*, 2015)) exercise interventions, with the most common form of exercise interventions including isometric, resistance and aerobic exercise. Isometric exercise involves the isotonic contraction of muscle, for example keeping a dumbbell suspended mid-air for a period of time by keeping the muscles engaged (Shepherd *et al.*, 1981). In contrast, resistance exercise involves the concentric and eccentric contraction of a muscle against resistance (Spiering *et al.*, 2008). Therefore, the tone of the muscle keeps changing, for example during dumbbell curls whereby the bicep muscles constantly contract and extend repeatedly in intervals. Aerobic exercise refers to a continuous state of steady exercise (usually ≥ 30 minutes) whereby oxygen is the main source of energy, such as running, cycling or swimming.

Recently, a new mode of exercise, high-intensity interval training (HIIT), has become a prominent exercise choice world-wide. HIIT is characterised by short-duration exercise, consisting of short bursts (one to five minutes) of high-intensity exercise separated with intervals of active rest (slow-pace walking) (Weston *et al.*, 2014). A common example of HIIT includes sprinting from one point to another and walking back to the starting point to sprint again. Due to its fairly recent involvement in the literature of pain and sleep health, limited research on the effects of HIIT on these variables is available (Passos *et al.*, 2010; O'Leary *et al.*, 2017; Vitale *et al.*, 2017; Hakansson *et al.*, 2018; Mijwel *et al.*, 2018). The few studies that have assessed the effects of HIIT on pain or sleep health are described in detail in sections 1.2.1 and 1.2.2, below.

Exercise, in the form of various modalities, has shown to improve pain sensitivity (Koltyn, 2002; Naugle *et al.*, 2012) and sleep quality (Driver & Taylor, 2000; Chennaoui *et al.*, 2015). Consequently, exercise could be used as an inexpensive, non-pharmacological therapeutic treatment for the improvement of pain and sleep quality, comorbidities associated with overweight and obesity (Wright *et al.*, 2010; Vargas *et al.*, 2014). In this section I will describe in detail studies that have assessed the impact of exercise on pain sensitivity and sleep quality in sections 1.2.1 and 1.2.2.

1.2.1 The effects of exercise on pain perception

Exercise is a recognised non-pharmacological therapeutic treatment for chronic pain conditions, such as osteoarthritis and fibromyalgia (Golightly *et al.*, 2012; Macfarlane *et al.*, 2017) with the benefits of exercise lasting as long as 30 months after the cessation of exercise (Hurely *et al.*, 2012). As such, the Public Health Agenda Recommendations for Osteoarthritis and the European League Against Rheumatism emphasize the importance of exercise, more specifically moderate-intensity continuous training (MICT), for the improvement of chronic pain as reviewed by Macfarlane *et al.* (2017) and Callahan *et al.* (2019). Consequently, exercise as a non-pharmacological intervention may hold clinical importance for improving pain without the adverse effects associated with pharmacological treatments.

The concept that exercise reduces or improves pain perception is referred to as exercise-induced hypoalgesia (EIH) (Koltyn, 2002). EIH is assessed by measuring and comparing pain perception before and after exercise interventions (Koltyn, 2002). Pain perception is assessed by measuring pain thresholds, pain tolerances and/or pain intensity ratings using Likert scales (Joshi *et al.*, 2015), numerical scales (Kahl & Cleland, 2013), or visual analogue scales (Kahl & Cleland, 2013).

For clarity, an *increased* post-exercise pain threshold suggests that a greater stimulus is required to induce pain compared to the baseline. Similarly, an *increased* post-exercise pain tolerance suggests that a noxious stimulus could be tolerated for a longer duration compared to the baseline. *Decreased* post-exercise pain intensity ratings indicate that a noxious stimulus is rated less painful compared with baseline pain intensity levels. Thus, an increased post-exercise pain threshold and/or pain tolerance and decreased pain ratings is indicative of reduced pain

perception and, therefore, EIH. Literature pertaining to the effects of exercise on pain perception are reviewed below according to pain-free (section 1.2.1.1) and chronic pain populations (section 1.2.1.2).

1.2.1.1 Exercise-induced hypoalgesia (EIH) in pain-free populations

Studies have assessed experimental pain perception before and after various exercise modalities, including aerobic, isometric and dynamic resistance exercise interventions, over different durations, as shown in Table 1.2, below. To summarise briefly, acute and regular *aerobic* exercise interventions, by means of cycling and running with durations between 10- to 30 minutes, have yielded the most consistent reports of EIH (Gurevich *et al.*, 1994; Koltyn *et al.*, 1996; Sternberg *et al.*, 2001; Hoffman *et al.*, 2004; Meeus *et al.*, 2010; Jones *et al.*, 2014; O'Leary *et al.*, 2017). Compared to other exercise modalities and intensities, 30 minutes of MICT, such as cycling and running yields the greatest EIH effect size in pain-free populations (Naugle *et al.*, 2012).

EIH, in the form of increased pressure pain threshold and decreased pressure- and thermal pain ratings, has also been reported in pain-free men and women participating in acute *isometric* exercise (Koltyn *et al.*, 2001; Staud *et al.*, 2005; Hoeger Bement *et al.*, 2008, 2009; Lannersten & Kosek, 2010). In contrast, two studies have reported no change in pressure pain thresholds and ratings in men and women after acute equipment-based isometric exercise at low intensities (10- and 25% maximum voluntary contraction) and durations between two- and ten minutes, respectively (Kadetoff & Kosek, 2007; Hoeger Bement *et al.*, 2008). Thus, acute isometric EIH, similar to aerobic EIH, may be dependent on the intensity and duration of the exercise intervention. Perhaps a higher intensity (25% maximum voluntary contraction) for longer durations (≥ two minutes) may have reduced pain sensitivity, such as seen in other studies (Koltyn *et al.*, 2001; Hoeger Bement *et al.*, 2008; Lannersten & Kosek, 2010).

The research pertaining to the effects of *resistance* exercise on pain perception in pain-free adults is limited. The two studies conducted assessed acute equipment-based resistance exercise, with both reporting reduced pain sensitivity in the form of increased pressure pain threshold and reduced pressure pain ratings in men and women (Koltyn & Arbogast, 1998; Focht & Koltyn, 2009). Therefore, more research is needed to determine whether, in pain-free populations, the

effects of acute resistance exercise on pain is dependent on the exercise duration and intensity, as it is with acute aerobic and isometric exercise.

Table 1.2: Studies assessing experimentally-induced pain perception before and after exercise in pain-free populations

Reference	n (%female)	BMI	Exercise intervention (duration)	Pain parameter	Site of pain stimulus	Outcome
Gurevich *et al.* (1994)	30 (0%)	-	Step exercise at 63% VO_{2max} (12 minutes)	Pressure pain tolerance and rating	Finger	↑ pain tolerance, ↓ pain rating
Koltyn *et al.* (1996)	16 (22%)	-	Cycling at 75% VO_{2max} (30 minutes)	Pressure pain threshold	Finger	↑ pain threshold
Kemppainen *et al.* (1998)	8 (0%)	-	Cycling at increment intensity - 50, 100, 150, 200W (5-8 minutes per intensity)	Cold pain threshold	Hand	No effect
Koltyn & Arbogast (1998)	13 (86%)	-	Resistance exercise at 75% 1RM × 3 (10 repetitions) ~ 45 minutes	Pressure pain threshold and rating	Finger	↑ pain threshold and ↓ pain rating
Koltyn *et al.* (2001)	31 (52%)	-	Isometric hand grip (to exhaustion)	Pressure pain threshold	Finger	↑ pain threshold for women only
	31 (52%)	-	Isometric hand grip at 40-50% MVC (2 minutes)	Pressure pain threshold	Finger	↑ pain threshold for women only
Sternberg *et al.* (2001)	10 (50%)	-	Treadmill running at 85% HR_{max} (10 minutes)	Cold pain rating	Hand and forearm	↓ pain rating in women only
Vierck *et al.* (2001)	20 (50%)	26.9	Treadmill running at maximum-intensity to exhaustion (> 11 minutes)	Cold pain rating (wind-up)	Hand	↓ pain rating
Hoffman *et al.* (2004)	12 (58%)	24.8	Running at 75% VO_{2max} (10 minutes)	Pressure pain rating	Finger	No effect

Reference	n (%female)	BMI	Exercise intervention (duration)	Pain parameter	Site of pain stimulus	Outcome
	12 (58%)	24.8	Running at 75% VO_{2max} (30 minutes)	Pressure pain rating	Finger	↓ pain rating
	12 (58%)	24.8	Running at 50% VO_{2max} (30 minutes)	Pressure pain rating	Finger	No effect
Ruble *et al.* (2005)	10 (-)	24.0	Treadmill running at 75% VO_{2max} (30 minutes)	Heat and cold pain threshold	Thumb	No effect
Staud *et al.* (2005)	11 (100%)	-	Isometric handgrip at 30% MVC (1.5 minutes)	Heat pain rating	Forearm	↓ pain rating
Kadetoff & Kosek (2007)	17 (100%)	-	Isometric knee extension at 10% MVC (10 minutes)	Pressure pain threshold	Thigh and shoulder	No effect
Hoeger Bement *et al.* (2008)	27 (52%)	-	Isometric elbow flexion at maximal contraction (2-3 seconds) × 3	Pressure pain threshold and rating	Finger	↑ pain threshold and ↓ pain rating
	22 (50%)	-	Isometric elbow flexion at 25% MVC to exhaustion	Pressure pain threshold and rating	Finger	↑ pain threshold and ↓ pain rating
	22 (50%)	-	Isometric elbow flexion at 25% MVC (2 minutes)	Pressure pain threshold and rating	Finger	No effect
	22 (50%)	-	Isometric elbow flexion at 80% MVC (to exhaustion)	Pressure pain threshold and rating	Finger	↓ pain rating

Reference	n (%female)	BMI	Exercise intervention (duration)	Pain parameter	Site of pain stimulus	Outcome
Focht & Koltyn (2009)	21 (0%)	-	Resistance exercise at 75% 1RM × 3 (10 repetitions)	Pressure pain threshold and rating	-	↑ pain threshold and ↓ pain rating
Hoeger Bement *et al.* (2009)	20 (100%)	-	Isometric elbow flexion at 25% MVC (to exhaustion)	Pressure pain threshold and rating	Finger	↑ pain threshold and ↓ pain rating
Lannersten & Kosek (2010)	21 (100%)	-	Isometric knee extension at 20-25% MVC (5 minutes)	Pressure pain threshold	Shoulder and thigh	↑ pain threshold
Meeus *et al.* (2010)	31 (68%)	23.4	Cycling at increment intensities from 20-130W (60 seconds per intensity ~ 29 minutes)	Pressure pain threshold	Hand, arm, back and calf	↑ pain threshold
Jones *et al.* (2014)	12 (92%)	-	Cycling at 75% HRR (30 minutes) 3 times per week (6 weeks)	Ischaemic pain tolerance and pain rating	Arm	↑ pain tolerance but no effect on pain rating
	12 (92%)	-	Cycling at 75% HRR (30 minutes) 3 times per week (6 weeks)	Pressure pain threshold	Trapezius, bicep, thigh and shin	No effect
O'Leary *et al.* (2017)	10 (20%)	25.8	HIIT: Cycling at 50% Δ (5 minutes × 6-8 intervals) 3 times per week (6 weeks)	Ischaemic pain tolerance and rating	Arm	↑ pain tolerance but no effects on pain rating
Hakansson *et al.* (2018)	16 (0%)	29.0	HIIT: Cycling at 90% HR_{max} (1 minute ×10 intervals) 3 times per week (6 weeks)	Pressure pain threshold	Thigh, shin and trapezius	No effect

BMI: body mass index; HR_{max}: maximal heart rate; VO_{2max}: maximal oxygen consumption; MVC: maximal voluntary contraction; 1RM: 1-repetition maximum; HRR: heart rate reserve; ↑: increased; ↓: decreased; Δ: intensity between lactate threshold and maximal oxygen consumption; HIIT: high-intensity interval training; -: data not reported

Nevertheless, studies on resistance exercise show that intermittent exercise (exercise repeated in intervals separated with periods of rest), as opposed to continuous steady state exercise, can evoke EIH in pain-free populations (Naugle *et al.*, 2012). The observation that intermittent exercise can evoke EIH was followed by the investigation of HIIT (although HIIT does not always involve resistance exercise), which is also an intermittent exercise intervention. Studies have shown that HIIT produces a comparable and sometimes greater improvement in cardiorespiratory fitness and metabolic improvements compared to the gold-standard MICT (Gibala & Mcgee, 2008; Talanian *et al.*, 2019). Therefore, it was proposed that HIIT may serve as a more time-efficient and more effective alternative to MICT for improving pain (Tjonna *et al.*, 2008).

Studies using HIIT as an exercise intervention to study changes in pain perception in pain-free populations are limited (O'Leary *et al.*, 2017; Hakansson *et al.*, 2018), and have produced conflicting results, as summarised in Table 1.2. In one study, a 6-week supervised HIIT intervention using a cycle ergometer did not change pressure pain thresholds in 28 overweight men (Hakansson *et al.*, 2018). In contrast, improved tourniquet-induced ischaemic pain tolerance, but not ischaemic pain ratings, was reported in 20 healthy- to overweight men and women after a 6-week supervised HIIT intervention using a cycle ergometer (O'Leary *et al.*, 2017).

The observation that HIIT increased tourniquet-induced pain tolerance without improving the corresponding ischaemic pain intensity ratings, suggests that mechanisms other than EIH may improve ischaemic pain tolerance (Jones *et al.*, 2014; O'Leary *et al.*, 2017). One proposed mechanism includes the habituation of ischaemic pain during exercise (Jones *et al.*, 2014). For example, metabolic accumulations, such as lactate, potassium, and adenosine, are increased in the muscles during exercise, similar to the metabolic accumulations during tourniquet-induced ischaemia (Jones *et al.*, 2014). Therefore, post-exercise increased ischaemic pain tolerance may be an indication of habituation of the nociceptors to the noxious metabolic accumulations during exercise (Jones *et al.*, 2014). As such, HIIT, associated with great metabolic changes (Gibala & Mcgee, 2008), may cause a great enough noxious metabolic accumulation for the adaptation of nociceptors and, consequently, increased ischaemic pain tolerance as seen by O'Leary *et al.* (2017). However, more research is required to confirm this hypothesis.

More research on HIIT is required to assess its efficacy as a more time-efficient and effective intervention to reduce pain sensitivity in pain-free populations, compared to MICT. Studying the efficacy of HIIT to reduce pain perception in pain-free participants allows for an exercise-pain model which can be compared to exercise-pain models in which participants with chronic pain are used. Additionally, more research on HIIT is also required in pain-free females as no study has assessed the efficacy of HIIT on pain-free populations using an all-female study sample. Using an all-female sample in studies assessing EIH is important as more women suffer from chronic pain conditions in South Africa, compared to men (Shisana *et al.*, 2013).

1.2.1.2 Exercise-induced hypoalgesia in chronic pain populations

The hypoalgesic effects of acute exercise in populations with chronic pain have produced equivocal results, as displayed in Table 1.3. The discrepancies in results may be attributable to the different underlying pathologies of the study populations (Naugle *et al.*, 2012; Rice *et al.*, 2019). For example, patients with localised chronic pain, such as knee osteoarthritis and shoulder myalgia, have been shown in all but one study (Lannersten & Kosek, 2010), to exhibit EIH when muscles distant to the area of chronic pain are exercised (Hoffman *et al.*, 2005; Meeus *et al.*, 2010; Burrows *et al.*, 2014; Smith *et al.*, 2017; Mijwel *et al.*, 2018). While, when muscles close to the localised chronic pain are exercised, no EIH (Lannersten & Kosek, 2010; Burrows *et al.*, 2014) or even post-exercise *hyper*algesia (Christensen *et al.*, 2017) is observed. Consequently, EIH seems to be most prevalent in patients with localised pain, when remote muscles are exercised (Rice *et al.*, 2019).

In contrast to patients with localised chronic pain, data supports that patients with chronic widespread pain, with possible central sensitization, such as fibromyalgia and chronic fatigue syndrome, may not exhibit improvements in pain (Cook *et al.*, 2010; Lannersten & Kosek, 2010; Hoeger Bement *et al.*, 2011; Ickmans *et al.*, 2017; Smith *et al.*, 2017) or may even show exacerbated pain (Vierck *et al.*, 2001; Whiteside *et al.*, 2004; Staud *et al.*, 2005; Cook *et al.*, 2010; Meeus *et al.*, 2010; Van Oosterwijck *et al.*, 2010, 2012) following acute exercise (Rice *et al.*, 2019). However, others have reported the contrary, being that some patients with chronic widespread pain, more specifically fibromyalgia, display EIH (Kadetoff & Kosek, 2007; Newcomb *et al.*, 2011; Tour *et al.*, 2017). The inconsistent data across the studies indicate no

clear pattern for EIH, which elucidates the complexity of EIH, especially in chronic pain populations with fibromyalgia.

Although no clear pattern is observable for EIH in populations with chronic pain, a meta-analysis has shown that acute MICT, for at least 30 minutes, yields the greatest effect size for EIH in populations with chronic pain (Naugle *et al.*, 2012). More recently, Mijwel *et al.* (2018) set out to compare the effects of two *regular* exercise interventions on experimentally-induced pressure pain, measured before and after a 16-week intervention, in 240 women with breast cancer. The exercise interventions consisted of a combination of cycling HIIT, using a cycle ergometer, combined with either equipments-based resistance training or continuous cycling on a cycle ergometer (Mijwel *et al.*, 2018). The cycling HIIT intervention combined with resistance training improved pressure pain thresholds in the trapezius muscles, while the cycling HIIT with continuous cycling had no effect on pressure pain thresholds. Due to the combined exercise modalities, it is unclear whether the HIIT, the resistance training, or the combination of HIIT with resistance training account for the improved pressure pain thresholds observed.

Consequently, more research on the effects of HIIT on populations with chronic pain is required to determine whether HIIT may serve as a more time efficient and effective, hypoalgesic intervention, compared to MICT. Additionally, no study assessing HIIT in a pain-free or chronic pain population has determined the efficacy of a home-based HIIT intervention without the use of gym equipment; therefore, the efficacy of a home-based HIIT intervention, without the use of equipment for reducing pain sensitivity in pain-free and chronic populations should be studied. The implication of assessing a home-based, equipment-free intervention includes a more cost-effective intervention that can be performed at one's own determined time. Not only could exercise, more specifically HIIT, be a cost-effective, non-pharmacological intervention to reduce pain in pain-free and chronic pain populations, but could also also act as a non-pharmacological intervention to improve sleep quality as reviewed in the next section.

Table 1.3: Studies assessing experimentally-induced pain perception before and after exercise in chronic pain populations

Reference	n (%female)	BMI	Health status	Exercise intervention (duration)	Pain parameter	Site of pain stimulus	Outcome
Vierck *et al.* (2001)	10 (100%)	29.5	Fibromyalgia	Treadmill running at high-intensity (to exhaustion)	Cold pain rating (wind-up)	Hand	↑pain rating
Whiteside *et al.* (2004)	5 (20%)	-	Chronic fatigue syndrome	Treadmill running at incremental incline at 5 km/h (15 minutes)	Pressure pain threshold	Thumb web	↓ pain threshold
Hoffman *et al.* (2005)	8 (50%)	28.1	Chronic low back pain	Cycling at 70% VO_{2max} (20 minutes)	Pressure pain rating	Finger	↓ pain rating
Staud *et al.* (2005)	12 (100%)	-	Fibromyalgia	Isometric handgrip at 30% MVC (1.5 minutes)	Heat pain rating	Forearm	↑ pain rating
Kadetoff & Kosek (2007)	17 (100%)	-	Fibromyalgia	Isometric knee extension at 10% MVC (10 minutes)	Pressure pain threshold	Thigh and shoulder	Thigh: No effect Shoulder: ↑ pain threshold
Cook *et al.* (2010)	16 (0%)	30.0	Chronic muscle pain	Cycling, at high-intensity (30 minutes)	Heat pain threshold (thumb) and rating (forearm)	Thumb and forearm	↑ pain rating
	15 (-)	31.2	Chronic muscle pain	Cycling at 70% VO_{2max} (30 minutes)	Pressure pain threshold	Finger	No effect
Lannersten & Kosek (2010)	20 (100%)	-	Shoulder myalgia	Isometric shoulder rotation at 20-25% MVC (5 minutes)	Pressure pain threshold	Shoulder and thigh	No effect

Reference	n (%female)	BMI	Health status	Exercise intervention (duration)	Pain parameter	Site of pain stimulus	Outcome
	20 (100%)	-	Shoulder myalgia	Isometric knee extension at 20-25% MVC (5 minutes)	Pressure pain threshold	Shoulder and thigh	No effect
	20 (100%)	-	Fibromyalgia	Isometric shoulder rotation at 20-25% MVC (5 minutes)	Pressure pain threshold	Shoulder and thigh	No effect
	20 (100%)	-	Fibromyalgia	Isometric knee extension at 20-25% MVC (5 minutes)	Pressure pain threshold	Shoulder and thigh	No effect
Meeus *et al.* (2010)	26 (52%)	23.5	Chronic fatigue syndrome	Cycling at increment intensities from 20-130W (60 seconds per intensity)	Pressure pain threshold	Hand, arm, back and calf	↓ pain threshold
	21 (81%)	24.5	Chronic low back pain	Cycling at increment intensities from 20-130W (17-29 minutes)	Pressure pain threshold	Hand, arm, back and calf	↑ pain threshold
Van Oosterwijck *et al.* (2010)	22 (100%)	24.1	Chronic fatigue syndrome	Cycling at 75% HR_{max} (15 minutes)	Pressure pain threshold	Back, calf and hand	Back and calf: ↓ pain threshold
Hoeger Bement *et al.* (2011)	15 (100%)	-	Fibromyalgia	Isometric elbow flexion at maximal contraction (2-3 seconds) × 3	Pressure pain threshold	Finger	No effect
	15 (100%)	-	Fibromyalgia	Isometric elbow flexion at 25% MVC (to exhaustion)	Pressure pain threshold	Finger	No effect

Reference	n (%female)	BMI	Health status	Exercise intervention (duration)	Pain parameter	Site of pain stimulus	Outcome
	15 (100%)	-	Fibromyalgia	Isometric elbow flexion at 25% MVC (2 minutes)	Pressure pain threshold	Finger	No effect
Newcomb *et al.* (2011)	21 (100%)	-	Fibromyalgia	Cycling at 60-75% HR_{max} (20 minutes)	Pressure pain threshold, tolerance and rating	Finger	↑ pain threshold and tolerance and ↓ pain rating
	21 (100%)	-	Fibromyalgia	Cycling at preferred intensity ~ 45% HR_{max} (20 minutes)	Pressure pain threshold, tolerance and rating	Finger	↑ pain threshold and tolerance and ↓ pain rating
Van Oosterwijck *et al.* (2012)	22 (100%)	22.9	Whiplash-associated disorder	Cycling at 75% HR_{max} (15 minutes)	Pressure pain threshold	Thumb web, finger, calf and lower back	↓ pressure pain threshold
Burrows *et al.* (2014)	11 (55%)	25.5	Knee osteoarthritis	Upper body resistance exercise at 60% 1RM × 3 (10 repetitions)	Pressure pain threshold and tolerance	Neck, bicep, lower arm, hand, thigh, calf and knee	↑ pain threshold
	11 (55%)	25.5	Knee osteoarthritis	Lower body resistance exercise at 60% 1RM × 3 (10 repetitions)	Pressure pain threshold and tolerance	Neck, bicep, lower arm, hand, thigh, calf and knee	No effect
Christensen *et al.* (2017)	16 (63%)	24.4	Chronic neck pain	Resistance shoulder abduction against gravity × 6 (6 repetitions)	Pressure pain threshold	Neck, head and arm	↓ pain threshold
	9 (78%)	26.2	Whiplash-associated disorder	Resistance shoulder abduction against gravity × 6 (6 repetitions)	Pressure pain threshold	Neck, head and arm	↓ pain threshold

Reference	n (%female)	BMI	Health status	Exercise intervention (duration)	Pain parameter	Site of pain stimulus	Outcome
Ickmans *et al.* (2017)	26 (58%)	25.3	Whiplash-associated disorder	Cycling at 75% HR_{max} (to exhaustion)	Pressure pain threshold	Neck and calf	No effect
Smith *et al.* (2017)	18 (55%)	-	Whiplash-associated disorder	Isometric wall squat (to exhaustion)	Hot and cold pain threshold	Neck	↑ thermal pain threshold
	17 (55%)	-	Whiplash-associated disorder	Cycling at 75% HR_{max} (30 minutes)	Hot and cold pain threshold	Neck	No effect
Tour *et al.* (2017)	130 (100%)	28.0	Fibromyalgia	Isometric knee extension at 30% MVC (to exhaustion)	Pressure pain threshold	Shoulder	↑ pressure pain threshold
Löfgren *et al.* (2018)	46 (93%)	-	Rheumatoid arthritis	Isometric knee extension at 30% MVC (to exhaustion)	Pressure pain threshold	Upper back and glutes	↑ pressure pain threshold
Mijwel *et al.* (2018)	74 (100%)	24.9	Breast cancer	HIIT: cycling at RPE 16-18 (3 minutes × 3 intervals) **combined with** resistance exercise at 80% 1RM × 2-3 (8-12 repetitions) (16 weeks)	Pressure pain threshold	Trapezius and glutes	↑ pressure pain threshold in trapezius

Reference	n (%female)	BMI	Health status	Exercise intervention (duration)	Pain parameter	Site of pain stimulus	Outcome
	74 (100%)	24.9	Breast cancer	HIIT: cycling at RPE 16-18 (3 minutes × 3 intervals) **combined with** cycling at RPE 13-15 (20 minutes) (16 weeks)	Pressure pain threshold	Trapezius and glutes	No effect

BMI: body mass index; HR_{max}: maximal heart rate; VO_{2max}: maximal oxygen consumption; MVC: maximal voluntary contraction; 1RM: 1-repetition maximum; HIIT: high-intensity interval training; ↑: increased; ↓: decreased; RPE: rating of perceived exertion; -: data not reported

1.2.2 The effects of exercise on sleep quality

Exercise has been proposed to improve sleep quality (Youngstedt *et al.*, 1997; Driver & Taylor, 2000; Youngstedt & Kline, 2006; Chennaoui *et al.*, 2015; Kredlow *et al.*, 2015; Banno *et al.*, 2018). Studies from the last two decades (2000 – 2020) are reviewed in this section, and two review papers are referenced for studies published before 2000 (Youngstedt *et al.*, 1997; Driver & Taylor, 2000). The reviews focusing on publications prior to the year 2000 concluded that exercise-induced sleep improvements, in particular increased sleep duration and slow wave sleep and reduced REM sleep, are more prevalent and show greater benefits in the female population as well as individuals with sleep complaints and/or those who are aged 40 years old and older (Youngstedt *et al.*, 1997; Driver & Taylor, 2000). In addition, the authors of these reviews discuss the importance of the period of exercise (acute versus regular) for mediating exercise-induced sleep improvements (Youngstedt *et al.*, 1997; Driver & Taylor, 2000). More specifically, exercise-induced sleep improvements, such as increased slow wave sleep, are evident after *acute* MICT at 50-70% peak oxygen consumption (VO_{2peak}) for durations ≥ 2.5 hours, or high-intensity (75-80% VO_{2peak}) for durations ≥ 1.2 hours. Sleep improvements, such as increased sleep duration and slow wave sleep and reduced sleep onset latency and wake after sleep onset, are evident after *regular* (8- to 16 weeks) aerobic exercise (Driver & Taylor, 2000).

The authors also draw attention to confounding variables that may affect the outcomes of studies that assess the effects of exercise on sleep quality, including overtraining, light exposure, time of day of training and physical fitness (Youngstedt *et al.*, 1997; Driver & Taylor, 2000). For example, overtraining (high-intensity training ≥ two hours) increases wake after sleep onset with a reduction in REM sleep (Driver *et al.*, 1994). Additionally, exposure to bright light, such as exercising outdoors during daytime, have somnogenic effects (Campbell *et al.*, 1993) that have been found to outweigh the sleep benefits of exercise itself (Guilleminault *et al.*, 1995). Lastly, exercise-induced sleep changes vary amongst individuals of differing aerobic fitness (Horne, 1981). For example, fit participants (defined as participating in physical activity for ≥ three times per week for durations ≥ 20 minutes per session (Youngstedt *et al.*, 1997)) may exhibit no change in sleep quality after acute exercise (Driver & Taylor, 2000). Therefore, defining the fitness levels (aerobic capacity) of study populations are crucial for studying the effects of exercise on sleep quality.

Prior to the year 2000, 27 studies pertaining to the effects of exercise on sleep were published, which would have added excessively to the current literature review; hence, I will only focus on the most recent two decades. In this section I will comprehensively review studies post-2000 pertaining to the effect of exercise on sleep quality of pain-free and chronic pain populations according to the period of the exercise interventions used (acute versus regular exercise).

1.2.2.1 Acute exercise

Studies published after 2000 assessing the effects of acute exercise (defined as studies of a cross-sectional nature with an exercise regimen performed once) on sleep quality, measured before and after exercise, are summarised in Table 1.4. Sleep improvements after acute exercise are common in patients with poor sleep quality and/or sleep disorders (Esteves *et al.*, 2009; Passos *et al.*, 2010; Morita *et al.*, 2011). In one study, sleep improvements, in particular increased sleep duration, sleep efficiency and REM sleep with reduced wake after sleep onset, were observed in 22 men and women with periodic leg movements, after 50 minutes of acute cycling on a cycle ergometer (Esteves *et al.*, 2009). Similarly, an improvement in sleep duration and sleep depth were observed in 71 men and women with poor sleep quality, according to the PSQI, after two hours of forest walking (Morita *et al.*, 2011). In another study the authors compared three 50-minute acute interventions; treadmill running MICT, equipment-based resistance MICT and treadmill running HIIT, in three separate groups of 12 insomniac men and women, and found improved sleep quality, particularly increased sleep durations and sleep efficiency with reduced sleep onset latency, only after the running MICT intervention (Passos *et al.*, 2010). In addition to measuring sleep quality, Passos *et al.* (2010) measured sleep state anxiety (increased in insomniacs) at baseline and again at post-exercise immediately before sleep, and only reported improved anxiety after the running MICT intervention. As such, the authors proposed that the absence of sleep improvements after resistance MICT and treadmill HIIT are attributed to the absence of improved sleep state anxiety after both these acute exercise interventions (Passos *et al.*, 2010). Therefore, it may be suggested that although exercise-induced sleep improvements are prevalent in patients with sleep disorders, exercise-induced sleep improvements are not shown if the sleep state anxiety is not improved in patients with insomnia.

Table 1.4: Studies from 2000-2020 assessing the effects of acute exercise on subjective and objective sleep parameters

Reference	n (% females)	Age (mean)	BMI	Sleep health status at baseline	Exercise intervention (duration)	Sleep assessment technique	Outcome
Oda & Moriya (2001)	8 (0%)	23	-	-	Recreational underwater exercise (50 minutes)	PSG OSA	No effect
Esteves *et al.* (2009)	22 (64%)	46	-	PLM	Cycling at unknown intensity (50 minutes)	PSG	↑ sleep duration ↑ sleep efficiency ↓ WASO ↑ REM sleep
Passos *et al.* (2010)	12 (83%)	48	26.1	Insomnia	Moderate-intensity treadmill training (50 minutes)	PSG Sleep log	↓ sleep onset latency (PSG and log) ↑ sleep efficiency (log) ↑ sleep duration (log)
	12 (75%)	42	24.4	Insomnia	Moderate-intensity resistance training (50 minutes)	PSG Sleep log	No effect
	12 (83%)	42	23.4	Insomnia	HIIT: Running at VT-2 (10 minutes × 3 intervals)	PSG Sleep log	No effect
Bulckaert et al. (2011)	9 (56%)	23	22.6	Good (measured with PSQI)	Cycling at 65-70% HR_{max} (60 minutes)	PSG	↑ slow wave sleep
Morita *et al.* (2011)	71 (39%)	45#	-	Poor (measured with PSQI)	Forest-walking (120 minutes)	SMHSQ Actigraphy	↑ sleep duration (actigraphy) ↓ movement (actigraphy) ↑ sleep depth (SMHSQ) ↑ sleep quality (SMHSQ)

Reference	n (% females)	Age (mean)	BMI	Sleep health status at baseline	Exercise intervention (duration)	Sleep assessment technique	Outcome
Myllymäki *et al.* (2011)	11 (36%)	26	-	Good (measured with BNSQ)	Cycling to exhaustion at incremental intensity (average of 35 minutes)	PSG Actigraphy Self-rated	↑ non-REM sleep (PSG)
Flausino *et al.* (2012)	17 (0%)	27	25.0	Good (measured with PSQI)	Treadmill running at VT-1 (30 minutes)	PSG	↓ WASO ↑ sleep efficiency ↓ N1 sleep
	17 (0%)	27	25.0	Good (measured with PSQI)	Treadmill running at VT-1 (60 minutes)	PSG	↓ WASO ↓ N1 sleep
	17 (0%)	27	25.0	Good (measured with PSQI)	Treadmill running at 50% above VT-1 (30 minutes)	PSG	↓ WASO ↑ sleep efficiency ↓ N1 sleep
	17 (0%)	27	25.0	Good (measured with PSQI)	Treadmill running at 50% above VT-1 (60 minutes)	PSG	↓ WASO ↑ sleep efficiency ↓ N1 sleep
Myllymäki *et al.* (2012)	14 (0%)	36	24.2	-	Running at light-intensity (30 minutes)	Actigraphy VAS Self-rated	No effect
	14 (0%)	36	24.2	-	Running at moderate-intensity (30 minutes)	Actigraphy VAS Self-rated	No effect
	14 (0%)	36	24.2	-	Running at high-intensity (30 minutes)	Actigraphy VAS Self-rated	No effect

Reference	n (% females)	Age (mean)	BMI	Sleep health status at baseline	Exercise intervention (duration)	Sleep assessment technique	Outcome
	14 (0%)	36	24.2	-	Running at moderate-intensity (60 minutes)	Actigraphy VAS Self-rated	No effect
	14 (0%)	36	24.2	-	Running at moderate-intensity (90 minutes)	Actigraphy VAS Self-rated	No effect
Viana *et al.* (2012)	40 (0%)	68	25.2	-	Resistance training at 60% 1RM (50-60 minutes)	PSG	↓ WASO ↓ N1 sleep
Wong *et al.* (2013)	12 (75%)	25	23.2	Good (measured with PSQI)	Treadmill running at 45% VO_{2max} (40 minutes)	PSG	No effect
	12 (75%)	25	23.2	Good (measured with PSQI)	Treadmill running at 55% VO_{2max} (40 minutes)	PSG	No effect
	12 (75%)	25	23.2	Good (measured with PSQI)	Treadmill running at 65% VO_{2max} (40 minutes)	PSG	↑ light sleep (N1+N2 sleep)
	12 (75%)	25	23.2	Good (measured with PSQI)	Treadmill running at 75% VO_{2max} (40 minutes)	PSG	↑ light sleep (N1+N2 sleep)
Vitale *et al.* (2017)	23 (-)	22	23.1	-	HIIT: Running at 90-95% HR_{max} (4 minutes × 4 intervals)	Actigraphy	No effect

OSA: sleep assessment of Oguri-Shirakawa-Azumi; PSG: Polysomnography; WASO: wake after sleep onset; PLM: periodic leg movements; HR_{max}: maximum heart rate; SMHSQ: St. Mary's hospital sleep questionnaire; PSQI: Pittsburgh sleep quality index; BNSQ: basic Nordic sleep questionnaire; REM: rapid eye movement; VT: ventilatory threshold; N1: non-REM stage 1; N2: non-REM stage 2; VAS: visual analogue scale; VO_{2max}: maximal oxygen consumption; HIIT: high-intensity interval training; - not reported; # mean age not reported, manually calculated from data
Studies prior to the year 2000 have been reviewed by Youngstedt et al. (1997) and Driver & Taylor (2002)

In addition to patients with poor sleep quality or sleep disorders, exercise-induced sleep improvements are also prevalent amongst participants aged 40 years and older (Viana *et al.*, 2012), as described by Driver & Taylor (2000). More specifically, parameters indicating improved sleep quality, such as reduced wake after sleep onset, were observed after 50 minutes of equipment-based resistance training in 40 overweight men between the ages of 65 and 80 years (Viana *et al.*, 2012). The improvement of sleep quality may be attributed to the notion that sleep impairments, such as increased wake after sleep onset and insomnia, become increasingly prevalent with age (Phillips & Ancoli-Israel, 2001); therefore rendering the elderly with room for sleep improvements.

As opposed to exercise-induced sleep improvements in patients with poor sleep quality and the elderly, acute exercise does not improve sleep quality of physically fit participants (Myllymäki *et al.*, 2012; Vitale *et al.*, 2017). More specifically, one study compared an acute home-based running interventions of various intensities (light- moderate- and high-intensity) and durations (30-, 60- and 90 minutes) in 36 physically active, healthy-weight men, and observed no improvement in sleep quality (Myllymäki *et al.*, 2012). Similarly, another study reported no improvements in sleep quality of 23 physically active, healthy-weight men and women after an acute supervised running HIIT intervention (Vitale *et al.*, 2017). Because physically fit participants already reap the benefits of exercise (Horne, 1981), the absence of exercise-induced sleep improvements may be attributed to the notion that physically fit participants have little room for improvement (referred to as the ceiling effect) (Chennaoui *et al.*, 2015), compared to sedentary participants.

Opposing the ceiling effect, four studies showed an improvement in sleep quality in participants *without* sleep complaints (Bulckaert *et al.*, 2011; Myllymäki *et al.*, 2011; Flausino *et al.*, 2012; Wong *et al.*, 2013). One study used an acute treadmill running intervention at varied intensities and durations in 27 sedentary, overweight men with good sleep quality according to the PSQI, and found that all levels of intensity (ventilatory threshold 1 and 50% above ventilatory threshold 1) and durations (30- and 60 minutes) improved sleep quality (Flausino *et al.*, 2012). Another study also used an acute treadmill running intervention at varied intensities (45-, 55-, 65- and 75% VO_{2max}) for 40 minutes in 12 overweight men and women with good sleep quality, according to the PSQI, and reported improved sleep quality only after 65- and 75% VO_{2max}

(Wong *et al.*, 2013). Furthermore, increased slow wave sleep was reported in nine healthy-weight men and women with good sleep quality, according to the PSQI, after an acute 60-minute cycling intervention on a cycle ergometer (Bulckaert *et al.*, 2011). Moreover, 11 healthy-weight men and women with good sleep quality, according to the Basic Nordic Sleep Questionnaire, showed improved sleep quality, more specifically increased non-REM sleep duration, after cycling to exhaustion on a cycle ergometer (Myllymäki *et al.*, 2011).

Of the four studies contradicting the ceiling effect (Bulckaert *et al.*, 2011; Myllymäki *et al.*, 2011; Flausino *et al.*, 2012; Wong *et al.*, 2013), three studies required their participants to exercise three- to two hours *before* bedtime (Bulckaert *et al.*, 2011; Myllymäki *et al.*, 2011; Flausino *et al.*, 2012). These three studies support the findings of others (Horne & Staff, 1983; Horne & Moore, 1985), including a meta-analytic review (Youngstedt *et al.*, 1997), which have shown that exercising close to bedtime does not adversely affect sleep quality as previously proposed (Morin *et al.*, 1999), but may have beneficial effects, including increased slow wave sleep duration (Horne & Staff, 1983; Horne & Moore, 1985). The proposed mechanism suggests that increased body temperature, such as seen during exercise, will activate cooling mechanisms via the hypothalamus and, as such, corresponding sleep behaviour regulated by the hypothalamus (Harding *et al.*, 2018). Supporting this thermogenic hypothesis is a study in which no sleep improvements were observed in eight men (unknown BMI) after 50 minutes of exercise in the evening in a swimming pool (Oda & Moriya, 2001). The author suggested that the absence of improved sleep is attributed to the cool water temperature (28.9 - 31.5 °C) in which the exercise was performed, so that the core body temperature (rectal temperature) did not rise significantly during exercise (Oda & Moriya, 2001). Similarly, compared to running in normal- to hot conditions (wearing shorts and a vest) in the evening, running in cool conditions (running in a cool stream of air wearing dampened shorts and a vest) in the evening did not improve sleep quality in six physically fit women (Horne & Moore, 1985). Therefore, by exercising in cool conditions, such as in a swimming pool or in dampened clothing, body cooling mechanisms via the hypothalamus are reduced, compared to exercising in normal or hot conditions (Harding *et al.*, 2018), and the corresponding sleep improvements diminished (Oda & Moriya, 2001).

Given that obesity and poor sleep quality commonly co-exist (Gangwisch *et al.*, 2005; Ogretmenoglu *et al.*, 2005), it is interesting that no study has specifically recruited an overweight

or obese study population to assess the effects of acute exercise on sleep quality. In addition, according to an extensive literature search, including publications prior to the year 2000, Passos *et al.* (2010) and Vitale *et al.* (2017) are the only studies that assessed the effects of acute HIIT on the sleep quality of insomniacs and physically active individuals, respectively. Briefly, acute HIIT did not improve sleep quality of physically active individuals(Vitale *et al.*, 2017), strengthening the ceiling effect hypothesis, and did not improve state anxiety and, consequently, sleep quality of insomniacs (Passos *et al.*, 2010). Evidently, more research is required assessing the efficacy of acute HIIT to improve sleep quality in patients with poor sleep quality or sleep disorders, including insomnia, as well as individuals with good sleep quality.

1.2.2.2 Regular exercise

Studies from the last two decades investigating the effects of regular exercise (defined as an exercise regimen performed at least twice a week for a minimum of one week) on sleep quality have yielded inconsistent results (Table 1.5). The majority of studies have relied on various subjective measures of sleep, with very few having used PSG, or even actigraphy. The subjective measures include the validated Women's Health Initiative Insomnia Rating Scale (Levine *et al.*, 2005) and validated Insomnia Severity Index (Bastien *et al.*, 2001) for assessing symptoms and severity of insomnia; the validated PSQI (Buysse *et al.*, 1989), the validated Medical Outcomes Study sleep scale (Hays & Stewart, 1992; Viala-Danten *et al.*, 2008) and the non-validated Sleep Problem Index (Hays *et al.*, 2005) for assessing participants' perception of sleep quality; the validated Fatigue Severity Scale (Valko *et al.*, 2008) and validated Epworth sleepiness scale (Johns, 1992) for assessing the level of fatigue and daytime sleepiness, respectively; the non-validated Apnoea-hypopnoea index (Bittencourt *et al.*, 2001) for assessing symptoms and severity of sleep apnoea; and the non-validated Sleep Questionnaire and Assessment of Wakefulness (Miles, 1982) for the diagnosis of sleep disorders.

As detailed in Table 1.5, all but three studies (Elavsky & McAuley, 2007; Oudegeest-Sanders *et al.*, 2013; Pinniger *et al.*, 2013) assessing men and women 40 years and older, reported improvements in various objective and subjective sleep aspects, including increased PSG-assessed deep sleep and sleep duration as well as improved subjective sleep quality, after regular exercise, regardless of sleep quality status at baseline (good versus poor) (Naylor *et al.*, 2000; King *et al.*, 2002, 2008; Tworoger *et al.*, 2003; Frye *et al.*, 2007; Esteves *et al.*, 2009; Chen *et*

al., 2010; Reid *et al.*, 2010; Richards *et al.*, 2011; Hosseini *et al.*, 2011; Nguyen & Kruse, 2012; Kline *et al.*, 2012; Pinniger *et al.*, 2013; Karlsen *et al.*, 2017*b*; Irandoust & Taheri, 2018). These studies support the notion that exercise-induced sleep improvements are prevalent in men and women aged 40 years and older (Driver & Taylor, 2000). A possible explanation could be that, although some participants aged 40 years and older may rate their sleep quality as good (Naylor *et al.*, 2000; Hughes *et al.*, 2018), sleep impairments, such as sleep apnoea and restless legs syndrome, become more prevalent with increasing age (Ancoli-israel *et al.*, 1997), leaving them with a greater opportunity for sleep improvement.

In contrast, three studies assessing participants aged 40 years and older, did not report improved sleep quality after regular exercise (Elavsky & McAuley, 2007; Oudegeest-Sanders *et al.*, 2013; Pinniger *et al.*, 2013). More specifically, no exercise-induced sleep improvements were reported, according to the PSQI, in 164 middle-aged overweight women after both supervised walking MICT (60 minutes) and low-intensity yoga (90 minutes) for 16 weeks (Elavsky & McAuley, 2007). Also, after a 48-week moderate- to high intensity cycling intervention on a cycle ergometer, no sleep improvements were reported according to actigraphy, in 21 elderly healthy- to overweight men and women (Oudegeest-Sanders *et al.*, 2013). According to the authors, discrepancies in results may be attributed to most similar studies using "less reliable" subjective techniques compared to the objective actigraphy used by Oudegeest-Sanders *et al.* (2013, p. 63). Indeed, there is often little agreement between objective and subjective sleep measures (Hughes *et al.*, 2018). However, King *et al.* (2008) used a similar exercise intervention, with a similar study sample and a superior objective technique (home PSG recordings) in conjunction with subjective assessments, and did find that the exercise intervention resulted in various objective and subjective sleep improvements, including reduced sleep onset latency and wake after sleep onset.

Table 1.5: Studies from 2000-2020 assessing the effects of regular exercise on subjective and objective sleep parameters

Reference	n (% females)	Age (mean)	BMI	Sleep health status at baseline	Exercise intervention (duration)	Sleep assessment technique	Outcome
Naylor *et al.* (2000)	14 (64%)	75	-	Healthy according to PSG	Light activity - walking, ball catching (50 minutes) 7×per week (2 weeks)	PSG	↑ slow wave sleep
King *et al.* (2002)	45 (100%)	62	27.8	Poor according to PSQI	Brisk walking at moderate-intensity (30-40 minutes) 4×per week (48 weeks)	PSQI	↑ sleep quality
Tworoger *et al.* (2003)	87 (100%)	61	30.5	Poor according to WHIIRS	Aerobic exercise at 60-75% HR_{max} (45 minutes) 5×per week (48 weeks)	WHIIRS	↓ sleep onset latency
Elavsky & McAuley (2007)	164 (100%)	50	28.9	Poor according to PSQI	Walking at moderate-intensity (60 minutes) 3×per week (16 weeks)	PSQI	No effect
	164 (100%)	50	28.9	Poor according to PSQI	Iyengar yoga at low-intensity (90 minutes) 2×per week (16 weeks)	PSQI	No effect
Frye *et al.* (2007)	72 (75%)	69	29.0	-	Tai Chi (60 minutes) 5×per week (12 weeks)	PSQI	↑ sleep quality
	72 (75%)	69	29.0	-	Low impact exercise (60 minutes) 5×per week (12 weeks)	PSQI	↑ sleep quality

Reference	n (% females)	Age (mean)	BMI	Sleep health status at baseline	Exercise intervention (duration)	Sleep assessment technique	Outcome
King *et al.* (2008)	36 (67%)	55	27.1	Poor according to SQAW	Aerobic exercise at 60-85% HR_{max} (30 - 40 minutes) 5×per week (48 weeks)	Home PSG PSQI Sleep diary	↓ wake after sleep onset (PSG) ↓ N1 sleep duration (PSG) ↑ N2 sleep duration (PSG) ↓ sleep disturbance (PSQI) ↓ sleep onset latency (diary) ↑ feeling rested after sleep (diary)
Esteves *et al.* (2009)	11 (55%)	46	-	PLM	Cycling (50 minutes) 3×per week (24 weeks)	PSG	↑ sleep duration ↑ sleep efficiency ↑ REM sleep
Manzaneque *et al.* (2009)	33 (94%)	18-21	-	Poor according to PSQI	Qigong (30 minutes) 3×per week (4 weeks)	PSQI	↑ sleep duration
Chen *et al.* (2010)	55 (53%)	75	-	Poor according to PSQI	Yoga (70 minutes) 3×per week (24 weeks)	PSQI	↑ sleep quality ↑ sleep duration ↑ sleep efficiency ↓ sleep disturbance ↓ daytime dysfunction
Reid *et al.* (2010)	17 (94%)	62	26.5	Insomnia	Aerobic exercise (walking, running or cycling) at 75% HR_{max} (40 minutes) 4×per week (16 weeks)	Actigraphy PSQI	↑ sleep quality (PSQI) ↓ daytime sleepiness (PSQI)
Hosseini *et al.* (2011)	62 (48%)	51	24.4	Poor according to PSQI	Tai Chi (20-25 minutes) 3×per week (12 weeks)	PSQI	↑ sleep quality (PSQI)
Richards *et al.* (2011)	193 (60%)	82	-	Sleep apnoea, periodic limb movement syndrome	Resistance training and walking (60 minutes) 5×per week (7 weeks)	PSG	↑ sleep duration ↑ sleep efficiency ↑ non-REM sleep duration

Reference	n (% females)	Age (mean)	BMI	Sleep health status at baseline	Exercise intervention (duration)	Sleep assessment technique	Outcome
Kalak *et al.* (2012)	51 (53%)	18	22.0	-	Running at own pace (30-37 minutes) 5×per week (3 weeks)	PSG ISI Sleep logs	↑ sleep quality (log) ↓ insomnia score (ISI) ↓ N1 sleep duration (PSG) ↑ N3 sleep duration (PSG) ↑ N4 sleep duration (PSG) ↑ deep sleep duration (PSG) ↑ REM sleep duration (PSG) ↓ REM latency (PSG)
Kline *et al.* (2012)	151 (100%)	58	31.8	Poor according to MOSSS and SPI score	Cycling/running at 50% VO_{2max} (4KKW) 3-4 ×per week (24 weeks)	MOSSS SPI	↓ MOSSS and SPI score
	99 (100%)	58	31.8	Poor according to MOSSS and SPI score	Cycling/running at 50% VO_{2max} (8KKW) 3-4 ×per week (24 weeks)	MOSSS SPI	↓ MOSSS and SPI score
	95 (100%)	58	31.8	Poor according to MOSSS and SPI score	Cycling/running at 50% VO_{2max} (12KKW) 3-4 ×per week (24 weeks)	MOSSS SPI	↓ MOSSS and SPI score
Nguyen & Kruse (2012)	96 (50%)	69	24.1	Poor according to PSQI	Tai Chi (60-minute) (24 weeks)	PSQI	↑ sleep quality
Oudegeest-Sanders *et al.* (2013)	21 (91%)	69	25.1	-	Cycling at 70-85% HR_{max} (30 minutes) 3×per week (48 weeks)	Actigraphy	No effect
Pinniger *et al.* (2013)	18 (89%)	40	-	Insomnia and fatigued according to ISI and FSS score	Tango (60 minutes) (8 weeks)	ISI FSS	↓ insomnia score (ISI)

Reference	n (% females)	Age (mean)	BMI	Sleep health status at baseline	Exercise intervention (duration)	Sleep assessment technique	Outcome
	12 (83%)	40	-	Fatigued according to FSS	Circuit training (60 minutes) (8 weeks)	ISI FSS	No effect
(Karlsen *et al.*, 2017*b*)	13 (31%)	51	37.0	Sleep apnoea	HIIT: running 90-95% HR_{max} (4 minutes × 4 intervals) 2 × per week (12 weeks)	AHI ESS	↓ AHI score ↓ ESS score
Irandoust & Taheri (2018)	34 (100%)	47	33.4	Poor according to PSQI	HIIT: 35m sprints × 6 intervals, 3 × per week (1 week)	Actigraphy	↑ sleep quality

PSG: Polysomnography; OSA: sleep inventory of Oguri-Shirakawa-Azumi; Periodic limb movement; HR_{max}: maximum heart rate; PSQI: Pittsburgh sleep quality index; WHIIRS: Women's Health Initiative Insomnia Rating Scale; ISI: insomnia severity index; SQAW: Sleep Questionnaire Assessment of Wakefulness; REM: rapid eye movement; KKW: kilocalories per kilogram of bodyweight; MOSSS: Medical Outcomes Study sleep scale; SPI: sleep problem index; FSS: fatigue severity scale; N: non-REM stage; VO_{2max}: maximal oxygen consumption; HIIT: high-intensity interval training; AHI: apnoea-hypopnoea index; ESS: Epworth sleepiness scale; -: not reported
Studies prior to the year 2000 have been reviewed by Youngstedt et al. (1997) and Driver & Taylor (2000)

In agreement with Elavsky & McAuley (2007) and Oudegeest-Sanders *et al.* (2013), no exercise-induced sleep improvements were reported, according to the Insomnia Severity Index and Fatigue Severity Scale, in 12 middle-aged men and women after eight weeks of equipment-based resistance training (Pinniger *et al.*, 2013). The absence of sleep improvements in the study of Pinniger *et al.* (2013) may be attributed to methods of statistical comparisons. More specifically, the post-exercise sleep outcomes (Insomnia Severity Index and Fatigue Severity Scale) of the exercising group were compared to the post-exercise sleep outcomes of a non-exercising control group, with no report as to whether the baseline sleep measures were comparable between the groups. Therefore, if the control group maintained a good sleep quality and the exercising group (with poor baseline sleep quality according to the Fatigue Severity Scale) had an improved sleep quality, the statistical analyses may not have reflected as such.

Two studies have assessed the effects of regular exercise on sleep quality of young adults, from which both reported improved objective and subjective sleep assessments (Manzaneque *et al.*, 2009; Kalak *et al.*, 2012). Increased sleep durations, assessed by the PSQI, were reported in 33 young men and women with poor sleep quality, after a 4-week Qigong intervention (Manzaneque *et al.*, 2009). Similarly, increased PSG-assessed deep sleep and REM sleep duration of 51 healthy-weight young men and women was observed after a three-week supervised running intervention (Kalak *et al.*, 2012). The exercise-induced sleep improvements in adolescents may be attributed to poor sleep quality associated with adolescence, such as short sleep durations and reduced alertness during the day (Carskadon, 2011), such as seen in Manzaneque *et al.* (2009); therefore, allowing room for sleep improvements.

As with acute exercise, to date, only two studies have assessed the effects of a regular HIIT intervention on sleep quality, with both studies reporting objective and subjective sleep improvements in obese individuals (Karlsen *et al.*, 2017*b*; Irandoust & Taheri, 2018). In one study, a 12-week treadmill running HIIT intervention improved both the apnoea-hypopnoea index and Epworth sleepiness scale scores in 13 obese middle-aged men and women with sleep apnoea (Karlsen *et al.*, 2017*b*). In another study, sleep quality, assessed by actigraphy, was improved in 34 obese middle-aged women with poor sleep quality, measured by the PSQI, after a one-week supervised sprinting HIIT intervention (Irandoust & Taheri, 2018). More research on HIIT is required to determine wether the sleep improvements observed in both studies (Karlsen

et al., 2017*b*; Irandoust & Taheri, 2018) are attributed to the study populations having poor sleep quality and aged 40 years and older, and whether HIIT may be a suitable non-pharmacological intervention for improving sleep quality. Additionally, as with acute exercise, most studies assessing the efficacy of regular exercise, including HIIT, to improve sleep quality used supervised and/or equipment-based interventions, such as treadmills or cycle ergometers. Therefore, more research is required to determine the efficacy of a home-based exercise intervention, without the use of gym equipment, to improve sleep quality.

1.3 Rationale for the Study

More than half of the South African female population is either overweight or obese (Shisana *et al.*, 2013). Although it is unclear whether BMI, subcutaneous- or central adiposity contributes to obesity-related pain, studies have shown that central obesity, and not BMI, may be the primary mediator in obesity-related poor sleep quality (Grunstein *et al.*, 1993; Davidson & Patel, 2008; Theorell-Haglöw *et al.*, 2010; Ford *et al.*, 2014). Given that pain and poor sleep quality are commonly associated with overweight and obesity (Guh *et al.*, 2009), and that pain and poor sleep quality exhibit a reciprocal relationship in which poor sleep quality and increased pain sensitivity ensure maintenance and augmentation of one another, I aimed to find a sustainable, non-pharmacological intervention to break this perpetual cycle in a South African female population.

The most consistent exercise-induced improvements in pain and sleep quality are prevalent after MICT (Driver & Taylor, 2000; Naugle *et al.*, 2012). However, MICT requires time, usually a minimum of 30 minutes per exercise regimen per day (Driver & Taylor, 2000; Naugle *et al.*, 2012), and time is often limited in the modern-day life (Justine *et al.*, 2013). As a result, exercise interventions of short durations, yielding the same or greater benefits as the gold-standard MICT, are of interest. HIIT is a well-documented example of a short duration exercise regimen that has shown greater cardiometabolic improvements in a shorter time-span compared to MICT (Gibala & Mcgee, 2008; Talanian *et al.*, 2019). Studies on the effects of HIIT on pain sensitivity of healthy-weight and overweight men and women are limited and have yielded conflicting results (O'Leary *et al.*, 2017; Hakansson *et al.*, 2018; Mijwel *et al.*, 2018). Additionally, only a few

studies have assessed the effects of HIIT on sleep quality of obese men and women (Karlsen *et al.*, 2017*b*; Irandoust & Taheri, 2018), with both studies demonstrating significant improvements in sleep quality. Moreover, no study has assessed the efficacy of HIIT as an intervention to improve pain sensitivity and sleep quality in an overweight female population.

Evidently, more research is required before HIIT interventions may be prescribed as a non-pharmacological intervention for the management of pain and poor sleep quality, especially in overweight women. In addition, the few studies evaluating the efficacy of HIIT to improve pain and sleep quality have used supervised, equipment-based interventions. Given the weakening economic state and high unemployment rate of South Africa (Stats SA, 2020), many South Africans do not have access to gym equipment; therefore, the efficacy of a convenient home-based, equipment-free HIIT intervention to reduce pain and improve sleep quality is required.

1.4 Aim, Hypotheses and Objectives

The aim of the current study is to assess the efficacy of a 14-week home-based, equipment-free HIIT intervention to reduce pain sensitivity and improve sleep quality in overweight women compared to healthy-weight and non-exercising women, as well as assess the association of waist circumference and BMI on pain and sleep quality in a South African female population. I hypothesise that the 14-week HIIT intervention will reduce pain perception and improve sleep quality in overweight women, as well as reduce pain perception in healthy-weight women. Moreover, I hypothesise that waist circumference will be associated with both pain sensitivity and sleep quality. The primary objectives of this study are to compare the effects of a 14-week own-body resistance HIIIT intervention in healthy-weight and overweight women, compared to non-exercising healthy-weight and overweight women in the following parameters:

1. anthropometric measures, specifically body mass, BMI, body fat percentage, waist circumference, hip circumference, waist-to-hip ratio and maximal oxygen consumption;
2. experimental pain thresholds, in particular pressure-, thermal-, mechanical pain threshold, and experimental ischaemic pain ratings;
3. sleep quality (PSQI score).

Additional objectives were to establish whether:

4. baseline pain perception (pressure-, thermal-, mechanical pain threshold and ischaemic pain) and sleep quality (PSQI score) are different between healthy-weight and overweight women;
5. baseline waist circumference and BMI are associated with baseline experimental pain perception (pressure-, thermal-, mechanical pain threshold and ischaemic pain) and sleep quality (PSQI scores).

2. MATERIALS AND METHODS

2.1 Ethical Approval

Methods of this study conformed to the Declaration of Helsinki and were approved by the Human Research Ethics Committee at the University of the Witwatersrand (clearance number: M180253; Appendix I).

2.2 Participants

Female participants between the ages of 19 and 40 years were recruited between July 2018 and March 2020 in and around the University of the Witwatersrand via social media forums, including Facebook, and local advertisement, such as wall posters within the university and the university's student newspaper (Wits Vuvuzela). Volunteers who showed interest in the study were contacted via email and provided with an overview of the study (Appendix II).

Interested volunteers were required to provide written consent, after which a screening session was done at the Movement Physiology Lab, University of the Witwatersrand. During screening the overall health of each volunteer was assessed using standardised questionnaires including; the General Health Questionnaire (Goldberg & Hillier, 1979) to assess general psychological health; and the Physical Activity Readiness Questionnaire (Warburton *et al.*, 2011) to assess the ability of volunteers to partake in exercise. The inclusion criteria included physically inactive females, i.e., females participating in less than 150 minutes of moderate- to high intensity physical activity per week (Thivel *et al.*, 2018), assessed verbally and by means of a baseline activity diary. Physically active females, females meeting the physical activity guidelines of 150 minutes of moderate- to high intensity physical activity per week (Tremblay *et al.*, 2011), were excluded from the study. Volunteers were also asked to report any chronic pain (pain lasting more than six months). Volunteers with chronic pain were not excluded from the study. All eligible participants proceeded to the experimental phase following a brief explanation of the study methods.

2.3 Anthropometry and Aerobic Capacity

Anthropometric measures and aerobic capacity of each participant were collected at baseline (at the start of the study) and after the study intervention (14 weeks from baseline day). Anthropometric measures included the assessment of BMI, waist-to-hip ratio and body fat percentage, while VO_{2peak} was used as a measure of aerobic capacity. Body fat percentage was measured according to standard procedure (Durnin & Womersley, 1974). In brief, skinfold thickness (mm) was measured from four anatomical sites (right triceps, supra-iliac, sub-scapular and mid-thigh) using a skinfold calliper (Harpenden, United States). Three measurements were recorded from each site and an average was calculated. The sum of the four skinfold measurements were used to calculate body density (Durnin & Womersley, 1974):

$$1.0994921 - (0.0009929 \times \text{sum of skinfolds}) + (0.0000023 \times [\text{sum of skinfolds}]^2) - (0.0001392 \times \text{age})$$

Thereafter, body fat percentage was calculated using body density:

$$\left(\frac{4.95}{body\ density} - 4.50\right) \times 100$$

Height (m) and body mass (kg) were measured using a stadiometer (Seca, Germany) and scale (Mettler-Toledo, USA), respectively. BMI was calculated using the formula:

$$\frac{body\ mass\ (kg)}{[height\ (m)]^2}$$

Waist- and hip circumference were measured on the left side of each participant using a metric tape measure (cm). With participants standing in the anatomical position, waist circumference was measured with the tape horizontally above the hip bone, while hip circumference was measured with the tape horizontally around the broadest part of the hip. Waist-to-hip ratio was calculated using the formula:

$$\frac{waist\ circumference\ (cm)}{hip\ circumference\ (cm)}$$

Aerobic capacity, or VO_{2peak}, was assessed according to the standardised Balke-Ware procedure (Balke & Ware, 1959), using a treadmill, heart rate monitor (COSMED, Italy) and a gas analyser (COSMED Quark CPET, Italy). The standardised Balke-Ware protocol requires participants to walk on a treadmill at 5.3 km/h throughout the assessment. The incline of the treadmill, starting

from 0%, was increased by one level each minute throughout the assessment. Every three minutes during the assessment, participants were asked to rate their effort of exertion on the Borg scale of perceived exertion (Borg, 1998). The VO_{2peak} assessment was terminated at the point of exhaustion, as assessed by the following criteria; a rate of perceived exhaustion (RPE) ≥ 18 (Borg, 1998) heart rate close to predicted maximum heart rate (220 – age) and an R-quotient > 1.

During the extent of the VO_{2peak} assessment the COSMED gas analyser recorded the oxygen consumption (ml/min) for each breath. Concurrently, for each breath, heart rate was recorded. VO_{2peak} was calculated by identifying the highest oxygen consumption rate reached during the assessment, divided by body mass (ml O_2/kg/min) (Balke & Ware, 1959). The heart rate corresponding to the breath with the highest oxygen consumption rate was used as the maximum heart rate (HR_{max}). HR_{max} was recorded for each participant and used to calculate prescribed exercise intensities, further discussed in section 2.5.

2.4 Group Allocations

Participants were assigned to either a 'healthy-weight' (BMI < 25 kg/m^2) or 'overweight' (BMI ≥ 25 kg/m^2) group according to BMI (Figure 2.1). Obese participants (BMI ≥ 30 kg/m^2) were also assigned to the overweight group for simplicity. Healthy-weight and overweight participants were randomly subdivided, using the random number generator function from MS Excel (2016 v. 16.0), into exercising and non-exercising groups to yield the following study groups: overweight and healthy-weight exercising groups (O-HIIT and H-HIIT, respectively), and overweight and healthy weight non-exercising groups (O-nonHIIT and H-nonHIIT; Figure 2.1). Both non-exercising groups (O-nonHIIT and H-nonHIIT) served as the control for the exercising groups (O-HIIT and H-HIIT). The H-HIIT group also served as the respective healthy-weight control to O-HIIT.

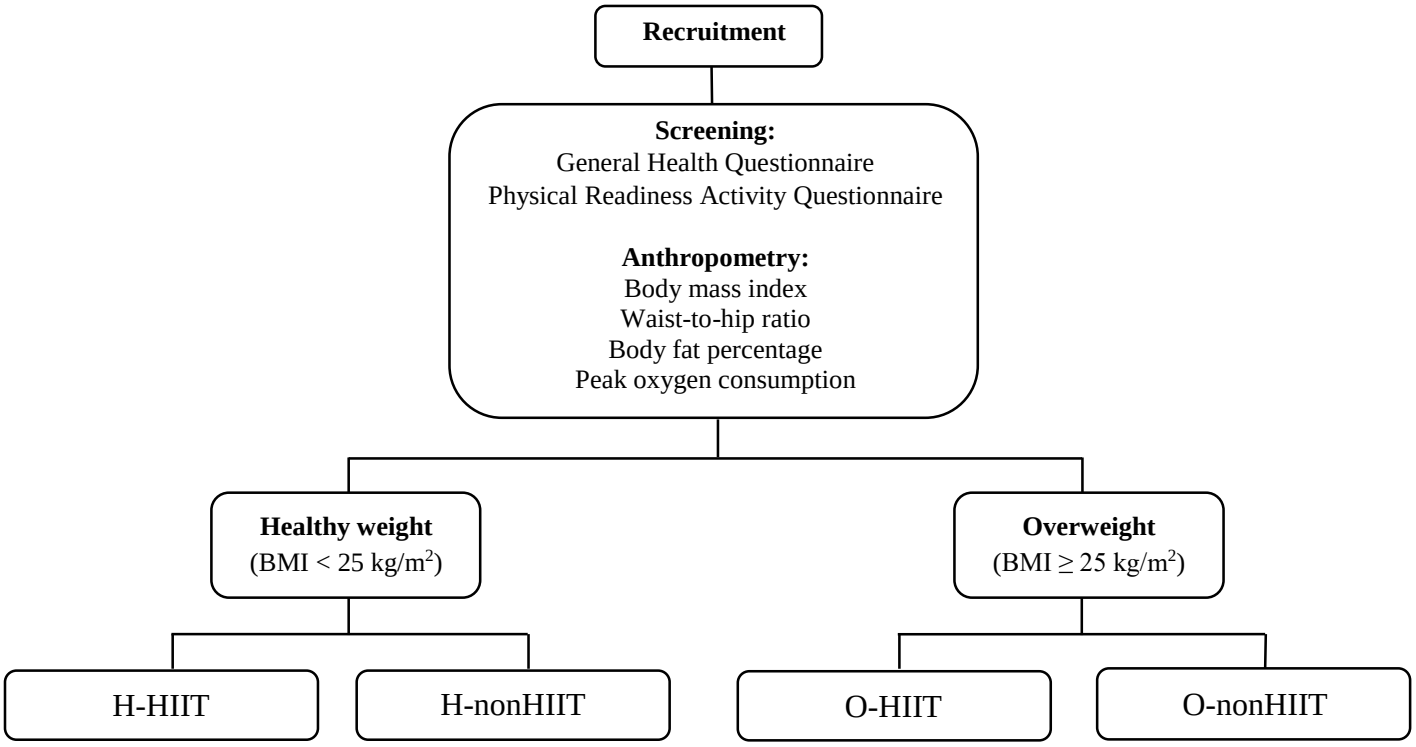


Figure 2.1: Group allocations of healthy-weight (H) and overweight (O) women into non-exercising (H-nonHIIT and O-nonHIIT) and exercising (H-HIIT and O-HIIT) groups. HIIT: high-intensity interval training.

2.5 Exercise Intervention, Intensities and Activity Diary

The study intervention took place over 14 weeks. During the 14-week intervention, non-exercising groups (H-nonHIIT and O-nonHIIT) maintained their habitual, physically inactive lifestyle. The exercising groups (H-HIIT and O-HIIT) followed a home-based HIIT intervention, six times per week at a prescribed intensity, over and above their habitual lifestyle. Furthermore, participants were permitted to perform the intervention any time of the day, no more than twice a day, i.e. once a day, six times per week or twice a day, three times per week.

The HIIT intervention consisted of intermittent combinations of own-body resistance exercise performed at high-intensity (Karlsen *et al.*, 2017*a*). Each combination included four own-body resistant exercises (e.g., squat jumps, lunges, burpees and high knees), performed for 30 seconds each to give a total of two minutes per combination (Appendix III). Overall, the HIIT intervention consisted of four combinations, two minutes per combination (2 minutes x 4 combinations). Each combination was separated by a one-minute period of active rest so that the overall HIIT intervention consisted of 11 minutes. These exercises were demonstrated to the participants by a research investigator (Zianca Smit) at baseline and, thereafter, performed without supervision.

The HIIT intervention was required to be performed at a pre-determined prescribed intensity as a percentage of each participant's HR_{max} (% HR_{max}), recorded during the VO_{2peak} assessment at baseline (Section 2.3). During the two-minute exercise combinations, participants were required to reach 85-95% HR_{max}. During the one-minute periods of active rest participants were required to maintain their heart rate at 65% HR_{max}. While performing the HIIT intervention, heart rates were monitored using personally owned activity watches with a heart rate function. Participants who did not have access to activity watches were given a Borg scale and were required to reach an exercise intensity equivalent to 16-17 RPE and an active rest intensity of 12-13 RPE (Borg, 1998). A Borg scale from 16-17 RPE is equivalent to that of 85-95% HR_{max}, and 12-13 RPE is equivalent to 65% HR_{max} (Garber *et al.*, 2011).

In addition, each participant was required to keep a daily activity diary in which they reported adherence to their assigned intervention (HIIT intervention or maintaining habitual, sedentary activity). Participants from the HIIT groups (H-HIIT and O-HIIT) were asked to exercise six-times per week for 14 weeks (84 sessions). Participants from the control groups (H-nonHIIT and O-nonHIIT) were required to maintain their physically inactive lifestyle and to report any activity participated in beyond their habitual activity. Furthermore, during the 14-week intervention participants were scheduled for in-person follow-ups every fourth week from baseline (week 4, 8 and 12 of the intervention) to remind participants to complete their activity diaries and to motivate the exercising participants.

2.6 Pain Perception and Mechanical Detection Threshold Assessment

To determine whether the 14-week HIIT intervention affects pain perception, pain thresholds and perception of experimental ischaemia were measured in all four study groups (H-HIIT, H-nonHIIT, O-HIIT and O-nonHIIT), before and 48 hours after the 14-week intervention to control for possible acute effects of exercise. The order in which the pain thresholds and experimental ischaemia were measured were randomised. Touch, or mechanical detection thresholds, were assessed according to standard procedure (Rolke *et al.*, 2006) to assess changes to the general somatosensory system (i.e. any innocuous changes following the 14-week intervention).

2.6.1 Experimental pain assessments

Pain thresholds (cold-, hot-, pressure- and mechanical pain threshold) were assessed according to the quantitative sensory test (QST) on the dorsal left hand, except for pressure pain thresholds, which was assessed on the palm (thenar muscle) of the left hand (Rolke *et al.*, 2006). Consecutive pain threshold tests were done once any pain from the previous test had completely subsided.

To assess cold- and hot pain thresholds a rectangular thermode (Somedic SenseLab, Sweden) with a 2.5 cm x 5 cm contact plate was used to relay temperatures to the skin. The temperature of the thermode decreased for cold pain threshold (ranging from 32 °C to 4.9 °C), and increased for heat pain threshold (ranging from 32 °C to 50 °C) at a rate of 1 °C/second from baseline temperature (32 °C). Once the sensation of the decreasing or increasing temperature changed from cool or warm, respectively, to an additional sensation of "burning, stinging, drilling or aching" participants pressed a button held in the right hand (Rolke *et al.*, 2010, p. 8). The press of the button recorded the temperature electronically and immediately returned the temperature to baseline (32 °C). Cold- and heat pain thresholds were each measured three times, with a ten-second interval between each cold and heat pain assessment. An arithmetic mean was calculated for both cold- and heat pain thresholds (Rolke *et al.*, 2006).

Mechanical pain threshold was assessed using weighted pin prick stimulators (MRC System PinPricks, Germany) that deliver calibrated forces ranging from 8- to 512 mN. Using the method of limits, the pin pricks were applied perpendicularly to the skin to determine supra- (the weight of the pin prick that was perceived as sharp) and submaximal pricking thresholds (the weight of

the pin prick that was perceived as blunt). Mechanical pain threshold was recorded as the geometric mean calculated from six supra-thresholds and six submaximal thresholds (mN).

Pressure pain thresholds were assessed using a pressure algometer (Somedic SenseLab, Sweden) with a 1 cm^2 contact probe. Pressure was gradually increased to the left thenar muscle, with a cut-off pressure at 1750 kPa. Once the sensation changed from one of pressure (kPa) to an additional sensation of "burning, stinging, drilling or aching" the participant pressed a button held in the right hand and the corresponding pressure was recorded (Rolke *et al*., 2010, p. 16). Pressure pain threshold was measured three times and an arithmetic mean was calculated for each participant (Rolke *et al.*, 2006).

Deep muscle ischaemic pain was induced in the right forearm using the standardised submaximal effort tourniquet test (Maixner *et al.*, 1990). A tourniquet cuff positioned above the *cubital fossa* was inflated to 200 mmHg to occlude blood flow. Once the cuff was inflated the participants performed ten hand-grip contractions with their right hand, using a hand-grip dynamometer (Lafayette, Indiana, model: 78010), at 30% of their maximum hand-grip strength. Each hand-grip contraction lasted two seconds, followed by a two-second rest period. Thereafter, the cuff remained inflated for ten minutes. Every minute during the ten-minute period of induced ischaemia, participants rated the level of perceived pain intensity on a 100 mm VAS anchored from 'no pain' to 'worst pain ever felt' (Kahl & Cleland, 2013). Each VAS was on a separate sheet, such that participants had no reference to their previous pain ratings. Each pain rating (total of ten ratings) was plotted over time to calculate an area under the curve (AUC; mm/min) for each participant. The AUC represented the participant's perceived pain over the ten-minute sub-maximal effort tourniquet test. To ensure forearm ischaemia was achieved after performing the sub-maximal effort tourniquet test, Von Frey hair (OptiHair$_2$, Marstock Nervtest, Germany) assessments (Weinstein, 1962) were completed both before the cuff was inflated (pre-ischaemia) and after the ten minutes of cuff inflation (during ischaemia). Von Frey hairs, which are carrier-mounted 40 mm-long nylon monofilaments with varying diameters (0.30 – 0.45 mm) that exert varying forces (0.25 – 512 mN), were applied perpendicularly to the right index finger tip until the Von Frey hair buckled in the middle. Starting from the finest filament, increasingly thicker diameters were applied to the skin to determine the finest filament the participant could feel while blindfolded (Weinstein, 1962).

2.6.2 Mechanical detection threshold

Mechanical detection thresholds were measured in all four groups (H-HIIT, H-nonHIIT, O-HIIT and O-nonHIIT) to assess non-painful sensory function (touch) of the skin. Mechanical detection thresholds were assessed, according to the QST (Rolke *et al.*, 2006), using Von Frey hairs (OptiHair$_2$, Marstock Nervtest, Germany). The participants were blindfolded, and the Von Frey hairs, starting from 16 mN to 0.25 mN, were applied perpendicularly to the anterior skin surface of the dorsal left hand until the Von Frey hair buckled in the middle. Using the method of limits, both supra-threshold (force of the finest filament that could be felt) and submaximal threshold (force of the thickest filament that could not be felt) were determined. A geometric mean was calculated from six supra-thresholds and six submaximal thresholds (mN) for each participant (Rolke *et al.*, 2006).

2.7 Sleep Quality Assessment

Subjective sleep quality was assessed at baseline and 48 hours after the 14-week intervention in all four study groups (H-HIIT, H-nonHIIT, O-HIIT and O-nonHIIT) using the PSQI (Buysse *et al.*, 1989). The PSQI is a standardised sleep quality questionnaire that assesses the sleep quality of the past month. The PSQI consists of seven components; perceived sleep quality, sleep onset latency, sleep duration, sleep efficiency, use of sleep medication, sleep disturbance and daytime dysfunction. Each component of the PSQI was scored from zero to three, with a higher score indicating *poorer* sleep quality. All seven components were added to obtain a global score out of 21, where a score > 5 indicates poor sleep quality (Buysse *et al.*, 1989). Moreover, a PSQI score change ≥ 3 is considered a clinically important difference in sleep quality (Hughes *et al.*, 2009; Banno *et al.*, 2018).

2.8 Statistics

Data management and analysis was performed on GraphPad Prism 8.4.3 (USA, 2018) and SAS software, version 9.4 (SAS institute Inc., Cary, North Carolina, USA), with significance

threshold set at P<0.05. Parametric data are shown as mean (standard deviation) and non-parametric data are shown as median [interquartile range].

To ensure that age, general health status and prevalence of chronic pain were comparable between the study groups (H-HIIT, O-HIIT, H-nonHIIT and O-nonHIIT) at baseline, we ran a one-way analysis of variance (ANOVA) with a Tukey *post hoc* for parametric data, and a Kruskal-Wallis test with a Dunns *post hoc* for non-parametric data. An unpaired two-sided t-test was performed to assess the compliance between both exercising groups (O-HIIT versus H-HIIT).

Two-way repeated measures ANOVAs were used to assess the interaction of independent variables (exercise and time) on the following dependant variables; body mass, BMI, body fat percentage, waist- and hip circumference, waist-to-hip ratio, aerobic capacity, cold-, heat-, mechanical- and pressure pain thresholds, perception of pain during ischaemia (AUC), mechanical detection threshold and PSQI scores. A Bonferroni *post hoc* with adjusted *p*-value (to correct for multiple comparisons) was used to assess differences *within* the study groups (baseline versus post-intervention), which was only assessed when a significant interaction was observed for the two-way repeated measures ANOVA. A Tukey *post hoc* with adjusted *p*-value (to correct for multiple comparisons) was used to assess differences *across* the study groups at baseline to ensure differences in anthropometry (BMI, waist- and hip circumference and body fat percentage) between healthy-weight and overweight groups as well as to ensure similarity in aerobic fitness. More specifically, the anthropometric variables (BMI, waist- and hip circumference, body fat percentage and VO_{2peak}) of O-HIIT were compared to O-nonHIIT and H-HIIT, while H-nonHIIT were compared to H-HIIT and O-nonHIIT. Similarly, a Tukey *post* with adjusted *p*-value (to correct for multiple comparisons) *hoc* was used to assess the differences in pain perception (cold-, heat-, mechanical- and pressure pain thresholds, perception of pain during ischaemia), mechanical detection threshold and PSQI scores *across* the study groups at baseline to assess differences between healthy-weight and overweight groups. More specifically, pain perception (cold-, heat-, mechanical- and pressure pain thresholds, perception of pain during ischaemia), mechanical detection threshold and PSQI scores of O-HIIT were compared to those of O-nonHIIT and H-HIIT, while the H-nonHIIT served as the control for H-HIIT. The PSQI component scores (sleep quality, sleep onset latency, sleep duration, sleep

efficiency, sleep medication, sleep disturbance, daytime dysfunction) were only assessed in a two-way repeated measures ANOVA when the global score showed a significant interaction. To control for differences in age between the groups at baseline, age was added as a confounding variable in repeated-measures ANOVA in a separate model if differences were observed between groups. Variables that were not normally distributed were log transformed prior to inclusion in statistical analyses. Non-parametric data were log-transformed, except for PSQI scores (as the log of zero is undefined), which were treated as a continuous variable (Buysse *et al.*, 1989), a method used by other studies (King *et al.*, 2008; Flausino *et al.*, 2012).

A number needed to treat (NNT) was calculated for significantly improved outcomes using a two-sided Fisher's exact test, to test the clinical impact of HIIT. The NNT was rounded to the nearest whole number.

To assess the relationships of baseline variables with waist circumference and BMI, correlations were performed on the combined sample. Separate one-tailed Pearson's Correlations (r) were used to assess the relationship between baseline pain thresholds, perception of pain during ischaemia, mechanical detection threshold and waist circumference and BMI. Non-parametric data were log-transformed. To assess the relationship of baseline PSQI scores with waist circumference and BMI, a one-tailed Spearman's Correlation (r_s) was used. PSQI component scores were only assessed when the global score was significantly correlated with the study variable.

3. RESULTS

3.1 Attrition Rate and Compliance

Volunteers who were interested in participating in the study were asked to visit the Movement Physiology Research Lab (University of the Witwatersrand) for baseline assessments. Initially, 55 participants were enrolled in the study. During the course of the study, 17 participants withdrew (Figure 3.1) due to ill health and personal reasons, such as relocation and studying for examinations, with none of these reasons being attributed to adverse effects from the HIIT intervention. Therefore, 38 participants completed the study. On average, participants from the HIIT groups completed 69 (SD = 21) sessions of the prescribed 84 exercise sessions (average of 82% compliance), based on self-reported adherence in activity diaries. Compliance between the overweight and healthy-weight exercising groups were comparable (t_9 = 0.278; O-HIIT = 79% versus H-HIIT = 84%; p = 0.787).

3.2 General Health and Chronic Pain

Baseline-assessed general health questionnaire scores were comparable across all the groups (H_3 = 7.58, p = 0.056). The prevalence of chronic pain at baseline did not differ across the study groups (O-HIIT: 60%; O-nonHIIT: 50%; H-HIIT: 30%; H-nonHIIT: 29%; H_3 = 2.59, p = 0.460). Chronic low back pain was the most prevalent form of chronic pain reported by overweight participants, while both neck pain and low back pain were common pain complaints from healthy-weight participants.

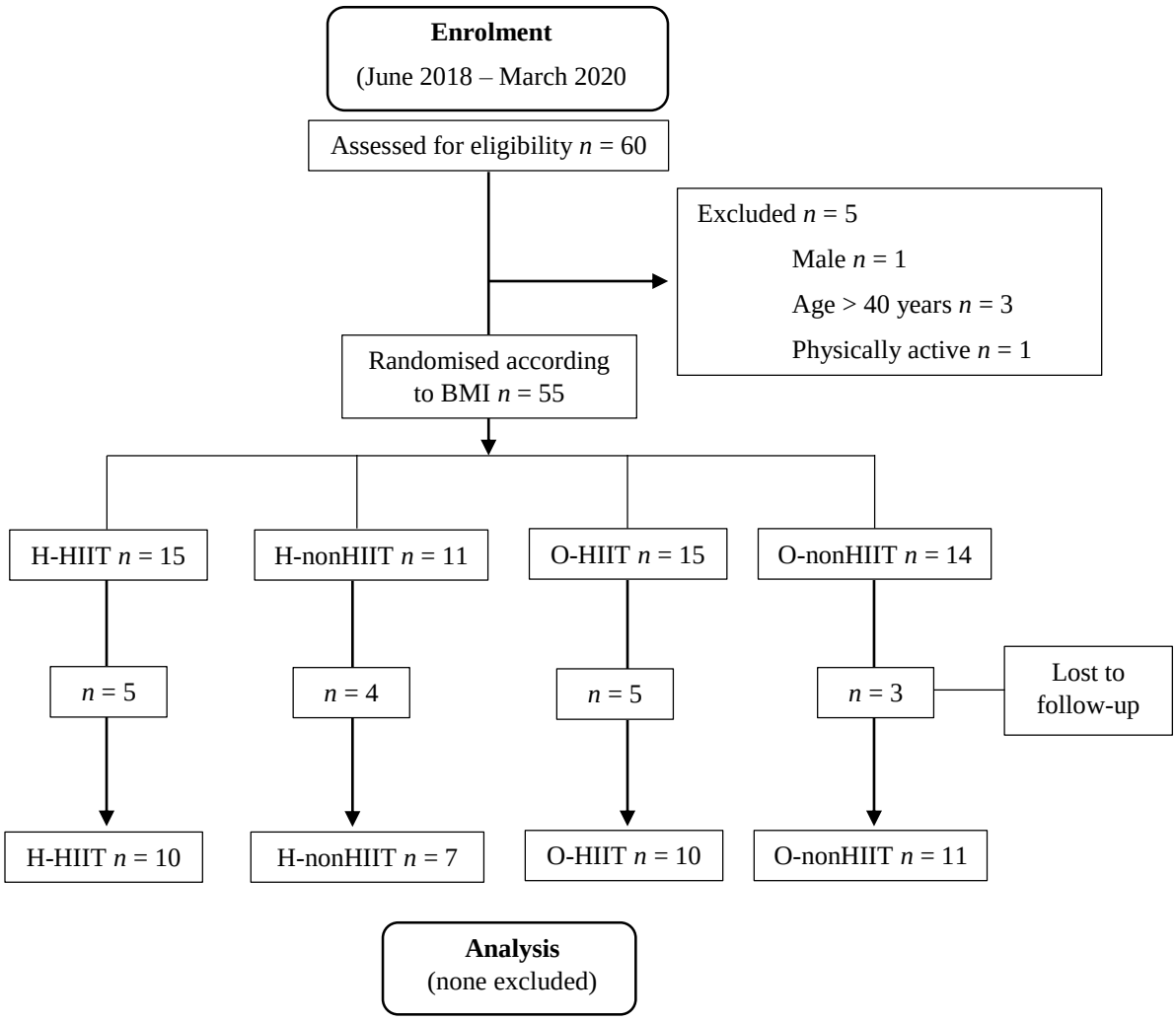


Figure 3.1: CONSORT flow diagram of the process of enrolment, eligibility and participants lost to follow-up, to the analysis of data.

3.3 Anthropometry

The population characteristics of each study group are summarised in Table 3.1. Age was not comparable across the group ($H_3 = 5.14$, $p = 0.005$). Anthropometry measured at baseline were different across the O-HIIT and H-HIIT group. Body mass, BMI, body fat percentage, waist- and hip circumference and waist-to-hip ratio was significantly greater in the O-HIIT group compared to the H-HIIT group ($p < 0.05$; Table 1.3). In addition, except for waist circumference and waist-

to-hip ratio, the O-nonHIIT group had a greater body mass, BMI, body fat percentage and hip circumference, compared to the H-nonHIIT group ($p < 0.05$; Table 1.3). Baseline VO_{2peak} levels were significantly higher in the H-HIIT group compared with the O-HIIT ($p < 0.05$). Body mass, BMI, body fat percentage, waist- and hip circumference and waist-to-hip ratio were comparable in the following groups: H-HIIT versus H-nonHIIT; and O-HIIT versus O-nonHIIT.

At 14 weeks, a two-way ANOVA showed a main effect for waist circumference ($p = 0.004$), with the *post hoc* showing reduced waist circumference at post-intervention compared to baseline in the O-HIIT group ($p < 0.001$; Table 3.1). A main effect was also shown for waist-to-hip ratio ($p = 0.031$); however, no *post hoc* differences were observed. After 14 weeks, no effect was observed for body mass, BMI, body fat percentage, hip circumference and VO_{2peak} in any of the study groups (Table 3.1).

Table 3.1: Study population demographics and anthropometry of healthy-weight (H) and overweight (O) exercising groups (H-HIIT and O-HIIT) and healthy-weight and overweight non-exercising groups (H-nonHIIT and O-nonHIIT) measured at baseline and post a 14-week high-intensity interval training (HIIT) intervention (n = 38)

	H-HIIT (n = 10)		**H-nonHIIT** (n = 7)		**O-HIIT** (n = 10)		**O-nonHIIT** (n = 11)	
	Baseline	*Post*	*Baseline*	*Post*	*Baseline*	*Post*	*Baseline*	*Post*
Age (years)	26 (7)	-	21 (1)	-	33 (7)	-	28 (7)	-
Body mass (kg) $F_{3,33} = 0.88$; $p = 0.460$	56.6 (8.7) α	56.4 (8.7)	58.9 (6.4) β	55.1 (9.3)	86.7 (13.4)	86.1 (12.5)	82.4 (13.7)	82.2 (14.0)
Body mass index (kg/m^2) $F_{3,33} = 0.76$; $p = 0.527$	22.1 (3.2) α	22.0 (3.0)	22.0 (3.0) β	20.8 (3.0)	33.0 (5.8)	32.8 (5.1)	30.7 (4.3)	30.7 (4.6)
Body fat (%) $F_{3,29} = 0.94$; $p = 0.435$	33.8 (5.3) α	33.0 (5.1)	30.6 (4.1) β	29.3 (5.0)	44.2 (4.4)	44.3(4.3)	41.6 (4.0)	41.6 (4.3)
Waist circumference (cm) $F_{3,27} = 5.76$; $p = 0.004$	76.0 (10.9) α	77.2 (9.5)	81.0 (6.3)	76.7 (4.3)	112.9 (21.7)	101.3 (18.6)**	95.7 (13.2)	98.6 (12.8)
Hip circumference (cm) $F_{3,27} = 2.79$; $p = 0.060$	96.2 (6.9) α	96.0 (6.9)	96.8 (6.3) β	99.6 (6.6)	120.6 (13.3)	116.6 (12.7)	115.3 (8.6)	115.4 (10.3)
Waist-to-hip ratio $F_{3,27} = 3.42$; $p = 0.031$	0.80 (0.1) α	0.80 (0.1)	0.84 (0)	0.77 (0)	0.91 (0.1)	0.87 (0.1)	0.83 (0.1)	0.85 (0.1)
VO_{2peak} (ml O_2/kg/min) $F_{3,30} = 0.053$; $p = 0.984$	28.2 (7.1) α	27.0 (5.6)	26.5 (3.1)	25.5 (3.0)	21.1 (7.4)	19.3 (4.9)	22.0 (3.3)	20.9 (4.0)

Data are shown as mean (SD); VO_{2peak}: peak oxygen consumption; F: two-way repeated measures ANOVA *within* groups comparing baseline to post-intervention, with corresponding p-values; **: $p < 0.001$ baseline vs. post intervention according to Bonferroni *post hoc*; α: vs. O-HIIT baseline ($p < 0.05$) according to Tukey *post hoc*; β: vs O-nonHIIT baseline ($p < 0.05$) according to Tukey *post hoc*

3.4 Experimental Pain Perception and Mechanical Detection Threshold

Pain thresholds (thermal, mechanical and pressure), experimental ischaemia and mechanical detection thresholds, measured before and after the 14-week exercise intervention, are summarised in Table 3.2. At baseline, cold pain threshold ($F_{3,29} = 0.25$, $p = 0.860$), heat pain threshold ($F_{3,29} = 0.011$, $p = 1.000$), mechanical pain threshold ($F_{3,32} = 0.19$, $p = 0.903$), pressure pain threshold ($F_{3,32} = 1.43$, $p = 0.251$), perception of pain during ischaemia ($F_{3,22} = 0.28$, $p = 0.839$) and mechanical detection threshold ($F_{3,23} = 1.49$, $p = 0.243$) were comparable across the study groups.

At 14 weeks, a main effect was observed for cold pain threshold ($p = 0.016$), heat pain threshold ($p = 0.043$) and mechanical detection threshold ($p = 0.005$; Table 3.2). *Post hoc* analyses showed that, in both overweight groups (O-HIIT and O-nonHIIT) a higher temperature was perceived as painfully cold (increased sensitivity to cold pain) after the intervention, compared to baseline ($p < 0.05$; Table 3.2). Therefore, cold pain sensitivity was increased in both O-HIIT and O-nonHIIT, suggesting cold pain hyperalgesia. No *post hoc* difference was observed for heat pain threshold and mechanical detection threshold. Age did not adjust the outcome for cold-, heat-, mechanical- and pressure pain threshold and perception of pain during ischaemia.

Table 3.2: Pain thresholds, ischaemic pain ratings and mechanical detection threshold from healthy-weight (H) and overweight (O) exercising groups (H-HIIT and O-HIIT) and healthy-weight and overweight non-exercising groups (H-nonHIIT and O-nonHIIT) measured at baseline and post a 14-week high-intensity interval training (HIIT) intervention

	H-HIIT			**H-nonHIIT**			**O-HIIT**			**O-nonHIIT**		
	n	*Baseline*	*Post*	*n*	*Baseline*	*Post*	*n*	*Baseline*	*Post*	*n*	*Baseline*	*Post*
CPT(°C) $F_{3;29} = 4.05$; $p = 0.016$	10	10.8 [6.1-16.1]	11.0 [4.9-15.9]	6	16.5 [10.5-17.0]	12.8 [7.6-22.1]	7	6.9 [5.2-9.9]	12.3 [10.0-25.1]*	10	8.1 [5.5-12.3]	17.6 [10.7-20.9]*
HPT(°C) $F_{3;29} = 3.08$; $p = 0.043$	10	41.4 (4.5)	43.1 (3.3)	6	41.3 (3.2)	43.1 (1.7)	7	43.2 (3.7)	40.8 (3.7)	10	43.1 (2.6)	41.2 (2.7)
MPT (mN) $F_{3,32} = 1.04$; $p = 0.388$	10	23.1 [15.2-56.0]	33.9 [19.7-65.4]	6	39.8 [28.1-107.3]	36.0 [20.3-55.3]	9	29.9 [24.3-97.0]	22.6 [17.1-27.9]	9	34.3 [26.6-66.3]	29.9 [16.8-48.6]
PPT (kPa) $F_{3,32} = 1.27$; $p = 0.302$	10	306 [267-328]	359 [283-396]	6	285 [217-328]	301 [251-380]	9	358 [286-419]	296 [282-391]	11	272 [225-296]	308 [279-324]
IPR (mm/min) $F_{3,22} = 0.66$; $p = 0.585$	8	467.3 (252.1)	449.2 (269.7)	4	487.5 (177.4)	563.2 (74.2)	5	527.2 (249.2)	483.5 (254.8)	9	519.8 (212.7)	575.4 (162.0)
MDT (mN) $F_{3;23} = 5.54$; $p = 0.005$	8	0.73 [0.46-1.32]	0.53 [0.21-0.86]	5	0.71 [0.71-1.23]	1.32 [1.32-3.03]	5	0.87 [0.44-1.32]	2.46 [1.74-2.64]	11	0.66 [0.30-1.41]	1.41 [0.56-1.87]

Parametric data are shown as mean (SD); non-parametric data are shown as median [IQR]
CPT: cold pain threshold; HPT: heat pain threshold; MPT: mechanical pain threshold; PPT: pressure pain threshold; IPR: ischaemic pain rating; MDT: mechanical detection threshold; F: 2-way repeated measures ANOVA within groups comparing baseline and post-intervention with corresponding *p*-values; *: $p<0.05$ vs. baseline according to Bonferroni *post hoc* test

3.5 Sleep Quality

Data from the PSQI, assessed at baseline and after the 14-week HIIT intervention, are shown in Table 3.3. Twenty-seven of the 38 participants completed the entire PSQI, whereby 11 questionnaires had incomplete sections and could, therefore, not be analysed. The PSQI global ($F_{3;23} = 0.64$, $p = 0.599$), sleep quality ($F_{3;23} = 0.52$, $p = 0.672$), sleep onset latency ($F_{3;23} = 1.25$, $p = 0.315$), sleep duration ($F_{3;23} = 0.49$, $p = 0.693$), sleep efficiency ($F_{3;23} = 0.055$, $p = 0.983$), sleep medication ($F_{3;23} = 1.45$, $p = 0.255$), sleep disturbance ($F_{3;23} = 0.66$, $p = 0.584$) and daytime dysfunction scores ($F_{3;23} = 1.41$, $p = 0.264$) were comparable across the study groups at baseline.

A significant main effect was observed for the global PSQI score ($p = 0.047$); however, no *post hoc* differences were observed (Table 3.3). The component scores for the PSQI were analysed to determine the specific components that contributed to the significant main effect for the global PSQI score. No significant main effect was observed for sleep onset latency, sleep duration, sleep efficiency, sleep medication, sleep disturbance and daytime dysfunction. A significant main effect was observed for sleep quality ($p = 0.012$). *Post hoc* analyses showed that in the O-HIIT group, the 14-week HIIT intervention significantly improved sleep quality, compared to baseline ($p < 0.05$) (Table 3.3). Age did not adjust the outcome for PSQI scores.

For the global PSQI score in the O-HIIT group, NNT = 1.481 ~ 1, 95% CI [0.757 – 2.215]; $p = 0.032$. For the sleep quality score in the O-HIIT group, NNT = 1.667 ~ 2, 95% CI [0.841 – 3.671]; $p = 0.035$.

Table 3.3: Pittsburgh sleep quality index (PSQI) global and component scores measured in healthy-weight (H) and overweight (O) exercising groups (H-HIIT and O-HIIT) and healthy-weight and overweight non-exercising groups (H-nonHIIT and O-nonHIIT) measured at baseline and post a 14-week high-intensity interval training (HIIT) intervention (n = 27)

	H-HIIT (n = 8)		**H-nonHIIT** (n = 6)		**O-HIIT** (n = 5)		**O-nonHIIT** (n = 8)	
	Baseline	*Post*	*Baseline*	*Post*	*Baseline*	*Post*	*Baseline*	*Post*
Global $F_{3;23} = 3.08$; $p = 0.047$	4.9 (1.8)	4.6 (1.9)	6.0 (3.2)	4.7 (1.8)	8.0 (1.9)	5.4 (3.4)	4.9 (3.3)	6.0 (3.6)
Sleep quality $F_{3;23} = 4.56$; $p = 0.012$	0.9 (0.4)	1.0 (0.5)	1.5 (0.8)	0.8 (0.8)	1.8 (0.8)	0.8 (0.4)*	0.9 (0.6)	1.1 (0.8)
Sleep onset latency $F_{3;23} = 0.42$; $p = 0.738$	1.0 (0.5)	0.6 (1.1)	1.2 (1.5)	0.7 (0.8)	1.6 (1.3)	1.6 (0.9)	0.8 (0.7)	0.8 (0.9)
Sleep duration $F_{3;23} = 0.81$; $p = 0.503$	1.1 (0.8)	1.0 (0.9)	1.0 (1.1)	0.8 (0.8)	1.6 (0.9)	0.8 (0.8)	1.4 (0.9)	1.4 (0.7)
Sleep efficiency $F_{3;23} = 1.40$; $p = 0.269$	0 (0)	0.1 (0.4)	0.2 (0.4)	0 (0)	0.2 (0.4)	0 (0)	0 (0)	0.1 (0.4)
Sleep medication $F_{3;23} = 0.45$; $p = 0.720$	0 (0)	0 (0)	0 (0)	0 (0)	0.2 (0.4)	0.6 (0.9)	0.4 (1.1)	0.5 (0.9)
Sleep disturbance $F_{3;23} = 0.88$; $p = 0.467$	1.3 (0.5)	1.1 (0.6)	1.2 (0.4)	1.3 (0.5)	1.6 (0.5)	1.4 (0.5)	1.1 (0.4)	1.3 (0.5)
Daytime dysfunction $F_{3;23} = 1.25$; $p = 0.314$	0.9 (0.6)	0.9 (0.6)	1.2 (0.4)	1.3 (0.5)	1.0 (0)	0.6 (0.5)	0.6 (0.5)	1.0 (0.8)

Data are shown as mean (SD); F: 2-way repeated measures ANOVA within groups comparing baseline and post-intervention with corresponding p-values; * $p < 0.05$ vs. baseline according to Bonferroni *post hoc* test

3.6 Association between Baseline Waist Circumference, Body Mass Index and Pain Perception and Sleep Quality

3.6.1 Baseline pain perception correlation with waist circumference and body mass index

No correlation was observed between baseline-assessed waist circumference and cold-, heat-, mechanical- and pressure pain thresholds and perception of pain during ischaemia in the combined sample (Table 3.4). No correlation was observed between baseline-assessed BMI and cold-, mechanical- and pressure pain threshold and perception of pain during ischaemia in the combined sample (Table 3.5). A positive correlation was shown between BMI and heat pain threshold ($p = 0.042$) in a combined sample (Figure 3.1), where a higher BMI was associated with higher heat pain thresholds, and therefore, decreased heat pain sensitivity.

Table 3.4: Pearson's Correlation between baseline-assessed waist circumference and pain perception in women partaking in an exercise intervention study

	Cold pain threshold	Heat pain threshold	Mechanical pain threshold	Pressure pain threshold	Ischaemic pain rating
n	28	28	30	30	26
r	0.267	0.253	0.183	0.0902	0.0341
p	0.085	0.097	0.167	0.318	0.434

Table 3.5: Pearson's Correlation between baseline-assessed body mass index and pain perception in women partaking in an exercise intervention study

	Cold pain threshold	Mechanical pain threshold	Pressure pain threshold	Ischaemic pain rating
n	34	36	36	26
r	0.214	0.202	0.214	0.147
p	0.113	0.119	0.106	0.237

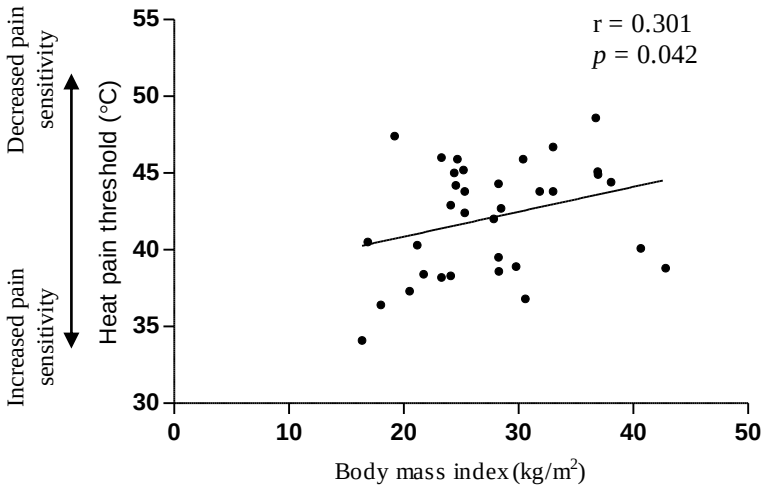
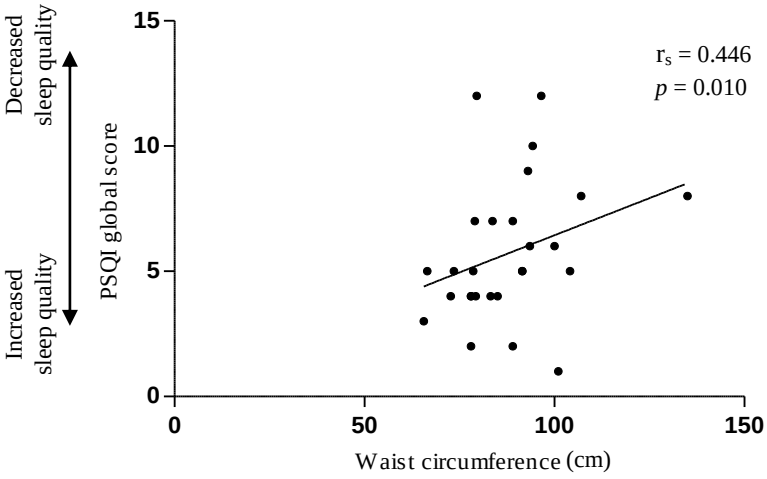


Figure 3.2: Pearson's Correlation between body mass index and heat pain threshold measured at baseline in women partaking in an exercise intervention study (n = 34).

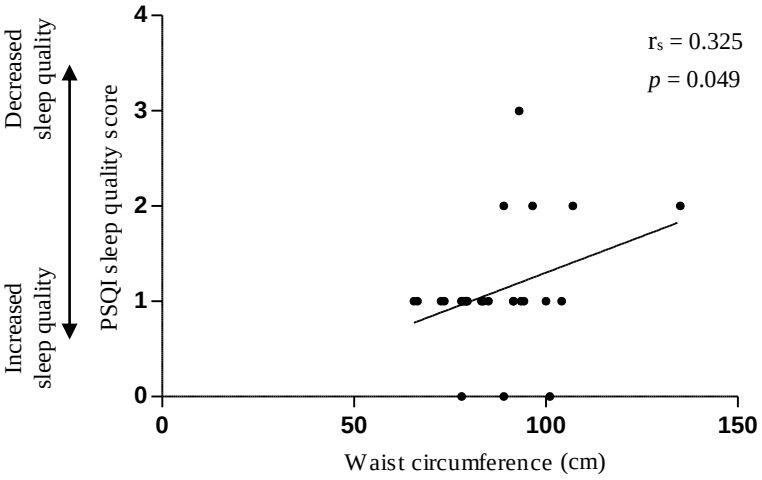
3.6.2 Baseline sleep quality correlation with waist circumference and body mass index

A positive correlation was observed between baseline-assessed waist circumference and PSQI global score in the combined sample (n = 27), where a larger waist circumference was associated with a higher PSQI score, indicating poorer sleep quality ($p = 0.010$; Figure 3.2 A). Individual component scores were analysed to determine which components may contribute to the correlation between the global score and waist circumference. Positive correlations between waist circumference were observed with the sleep quality scores (p = 0.049; Figure 3.2 B) and sleep duration scores ($p = 0.005$; Figure 3.2 C). No relationships were observed between waist circumference and sleep onset latency (r_s = 0.256, p = 0.099), sleep efficiency (r_s = 0.0727, $p = 0.359$), sleep medication (r_s = 0.238, $p = 0.116$), sleep disturbance (r_s = 0.299, p = 0.065) and daytime dysfunction (r_s = 0.120, $p = 0.275$). No correlation was observed between BMI and PSQI global score (r_s = 0.270, p = 0.086) in the combined sample (n = 27).

A


Decreased sleep quality
Increased sleep quality
PSQI global score
15
10
5
0
0
50
100
150
Waist circumference (cm)
r_s = 0.446
p = 0.010

B


Decreased sleep quality
Increased sleep quality
PSQI sleep quality score
4
3
2
1
0
0
50
100
150
Waist circumference (cm)
r_s = 0.325
p = 0.049

C

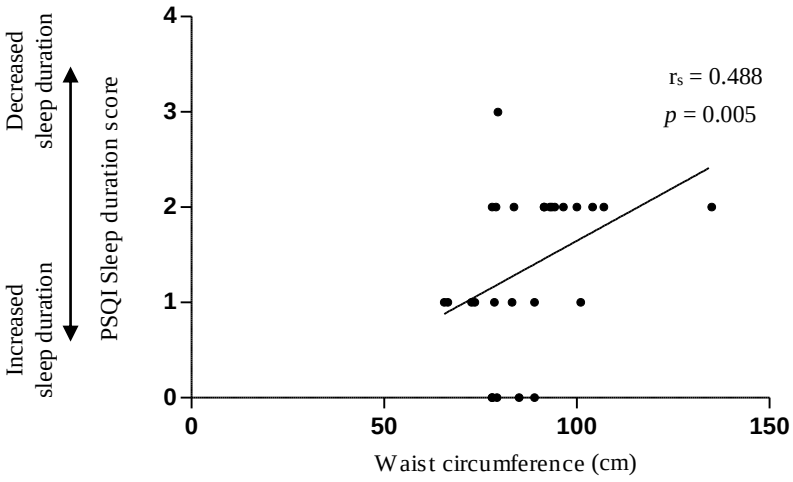


Figure 3.3: Spearman's Correlation between waist circumference and Pittsburgh sleep quality index (PSQI) global score (A), sleep quality score (B) and sleep duration score (C) measured at baseline in women partaking in an exercise intervention study (n = 27).

4. DISCUSSION

This dissertation is the first to assess the effects of a 14-week HIIT intervention on a battery of pain parameters, ranging from various pain thresholds (thermal, mechanical and pressure) to pain intensity over time (ischaemia), and sleep quality in healthy-weight and overweight women. I hypothesised that the 14-week HIIT intervention would reduce pain perception of healthy-weight and overweight women as well as improve sleep quality of overweight women. We found that the 14-week HIIT intervention effectively reduced the waist circumference of the overweight women, but not the healthy-weight women. The HIIT intervention did not alter body mass, body fat percentage, hip circumference, waist-to-hip ratio or VO_{2peak} in either the healthy-weight or the overweight women.

Pain perception at baseline did not differ between the healthy-weight and overweight women. Nevertheless, at baseline, reduced heat pain sensitivity was associated with increased BMI, but not waist circumference. The 14-week HIIT intervention did not alter experimental pain perception in either the healthy-weight exercising women or the healthy-weight non-exercising women. Similarly, with the exception of cold pain threshold, the 14-week HIIT intervention did not alter experimental pain perception in both the overweight exercising and the overweight non-exercising women. However, surprisingly, both these overweight groups experienced an increased sensitivity to cold pain after the 14-week HIIT intervention.

Sleep quality did not differ between overweight and healthy-weight women at baseline. However, at baseline an increased waist circumference, but not BMI, was associated with poorer sleep quality and reduced sleep durations in our sample as a whole. The 14-week HIIT intervention improved sleep quality in overweight women, but not healthy-weight women. No other subjective sleep component was altered after the 14-week HIIT intervention in any of the study groups.

The following sections discuss the results of my dissertation in context with what exists in the published literature. Due to the limited research available on HIIT, especially in a female population, the results will be discussed in context with the most relevant literature.

4.1 Compliance and the Effects of a 14-Week Exercise Intervention on Measures of Anthropometry and Aerobic Capacity

In the current dissertation 82% of the participants complied to the 14-week exercise intervention. A meta-analytic review showed that exercise-sleep studies using regular exercise have an average adherence rate of 84% (Kredlow *et al.*, 2015), while exercise-pain studies using regular exercise have adherence rates ranging from 75 – 100% (Jones *et al.*, 2014; O'Leary *et al.*, 2017; Hakansson *et al.*, 2018; Mijwel *et al.*, 2018). Therefore, compliance in this study is just below average. However, it should be noted that all of these exercise-sleep and exercise-pain studies used supervised exercise interventions which may account for their slightly higher adherence rates compared to the current study. Nevertheless, this study set out to assess the efficacy of a home-based, unsupervised exercise intervention and the adherence rate was comparable to that of lab-based, supervised studies. However, it is unclear whether participants in a home-based study exercise at the required intensities, compared to supervised participants where exercise intensity is monitored.

In the current study, differences in baseline body mass, body fat percentage, waist circumference, hip circumference, waist-to-hip ratio and VO_{2peak} between healthy-weight and overweight women are expected, given their classification according to BMI. Similar baseline waist-to-hip ratios between non-exercising healthy-weight and non-exercising overweight women likely indicate that the distribution of fat across the body is alike in both groups, possibly with a greater distribution around the waist given that in our sample, there was no difference in waist circumference between the non-exercising overweight and non-exercising healthy-weight women at baseline. Although VO_{2peak} was higher in the overweight exercising women compared to the healthy-weight exercising women, an aerobic capacity below 40 ml O_2/kg/min across the four groups confirm that the study sample of the current study was physically inactive/sedentary (Youngstedt *et al.*, 1997).

No changes in body mass were observed in either groups after the 14-week HIIT intervention. The results are in accordance with other studies assessing the effects of regular HIIT (6- to 12 weeks) on physiological parameters in healthy-weight (Chidnok *et al.*, 2020) and overweight women (Gillen *et al.*, 2016; Panissa *et al.*, 2016). The HIIT interventions employed by these studies had intermittent exercise bouts ≤ two minutes (Gillen *et al.*, 2016; Panissa *et al.*, 2016; Chidnok *et al.*, 2020), similar to the current study which entailed high-intensity own-body resistance exercise bouts lasting two minutes. In contrast, three studies have reported reduced

body mass, and hence BMI, in healthy-weight (Trapp *et al.*, 2008) and overweight women (Zhang *et al.*, 2015, 2017) after regular HIIT interventions spanning 12- to 15 weeks. However, Trapp *et al.* (2008) reported reduced body mass in healthy-weight women after a 15-week HIIT intervention, compared to a non-exercising group (Trapp *et al.*, 2008). Therefore, the body mass difference is between two different groups of women, rather than between baseline and post-exercise intervention, as measured in this study and done by Gillen *et al.* (2016), Panissa *et al.* (2016) and Chidnok *et al.* (2020). Nevertheless, Zhang *et al.* (2015, 2017) reported reduced body mass, and hence BMI, compared to baseline, in overweight women after a 12-week HIIT intervention consisting of a 4×4 minutes cycling intervention (~25 minutes) performed 4 times per week. As such, it is possible that the duration of the intermittent exercise bouts is what determines whether body mass will be altered; whereby intermittent exercise ≤ two minutes may not reduce body mass over a 12- to 15-week intervention period.

The current study also found no change in body fat percentage after the 14-weeks HIIT intervention in the overweight women, compared to baseline. The results are contrasted by several studies that have reported reduced body fat percentages after regular running and cycling HIIT interventions, between 6- to 12 weeks, in overweight women (Zhang *et al.*, 2015, 2017; Gillen *et al.*, 2016; Panissa *et al.*, 2016). Body fat percentage in these studies were assessed using body scans (Zhang *et al.*, 2015, 2017) and air-displacement methods (Gillen *et al.*, 2016), which may be considered more reliable than skin-fold measurements, and thus, may account for the inconsistent results between the current study and those that reported reduced body fat percentages. However, another study reported reduced body fat percentage, assessed in the same manner as this study; four skinfold measurements using skinfold calipers (Panissa *et al.*, 2016). It is possible that our findings of no change in body mass, and no change in percentage body fat following a 14-week HIIT intervention is due to the fact that we did not monitor food intake, nor did we ask partipants to change their habitual caloric intake (Panissa *et al.*, 2016). It is possible the participants compensated for increased energy expenditure (due to exercise) by increasing caloric intake (Poehlman *et al.*, 1990).

Similarly, body fat percentage of the healthy-weight women in this study did not decrease after the 14-week HIIT intervention. No study has assessed the effects of a regular HIIT intervention on body fat percentage of healthy-weight women; therefore, there are no directly comparable

studies. Nevertheless, it is possible that the absence of reduced body fat percentage in the healthy-weight women after the exercise intervention may also be attributed to a possible increased caloric intake to compensate for their increased energy expenditure.

Only one study has reported the effects of a regular HIIT intervention on waist circumference, hip circumference and waist-to-hip ratio in overweight women (Panissa *et al.*, 2016). Similar to the findings from the current study, Panissa *et al.* (2016) reported reduced waist circumference with no change in hip circumference in overweight women after a 6-week cycling HIIT intervention. Although muscle mass was not directly measured, a change in waist circumference in overweight women in conjunction with no change in weight or BMI, as seen in this study and the study of Panissa *et al.* (2016), may be indicative of increased muscle mass. Indeed, increased muscle mass is associated with short-duration high-intensity intermittent exercise in overweight men (Terzis *et al.*, 2008).

Contrary to my study results, a reduced waist-to-hip ratio was reported in overweight women after a 6-week HIIT intervention (Panissa *et al.*, 2016). The absence of reduced waist-to-hip ratios after the 14-week HIIT intervention may be attributed to the trend towards a reduced hip circumference in conjunction with a reduced waist circumference. Hence, the ratio between the waist- and hip circumference remain comparable between baseline and post-intervention. As such, the reduced waist-to-hip ratio reported by Panissa *et al.* (2016) may be attributed to a reduced waist circumference that did not parallel with a reduced hip circumference.

In this study, no changes were observed in waist circumference, hip circumference and waist-to-hip ratio in healthy-weight women after the 14-week HIIT intervention. No other study has assessed the effects of a regular HIIT intervention on anthropometric parameters of healthy weight females. Therefore, it is unclear how the results of the current study would compare to other healthy-weight females after a regular HIIT intervention.

In contrast, VO_{2peak} is well represented in studies assessing the effects of regular, 2- to 16-week HIIT interventions, in women (Zhang *et al.*, 2015, 2017; Gillen *et al.*, 2016; Panissa *et al.*, 2016; Mijwel *et al.*, 2018; Talanian *et al.*, 2019; Chidnok *et al.*, 2020). Contrary to the current study, several studies have reported increased VO_{2peak} in overweight (Zhang *et al.*, 2015, 2017; Gillen *et al.*, 2016; Panissa *et al.*, 2016) and healthy-weight women (Chidnok *et al.*, 2020) following

regular cycling and running HIIT interventions. Similar to the current study, Mijwel *et al.* (2018) did not observe increased VO_{2peak} in overweight women after a 16-week cycling HIIT intervention. The studies in which increased VO_{2peak} were seen had a participants compliance of ≥ 86% (Zhang *et al.*, 2015, 2017; Gillen *et al.*, 2016; Panissa *et al.*, 2016), with one study not reporting compliance (Chidnok *et al.*, 2020). In the current study and the study of Mijwel *et al.* (2018) in which no VO_{2peak} improvement was reported, compliance to the exercise intervention ranged between 75-83%. Therefore, an improved VO_{2peak} may be reliant on the compliance to a HIIT intervention stretching over 2- to 16 weeks. Additionally, the current study's exercise intervention was home-based and unsupervised. Therefore, it is possible that, although the participants reported exercising, they may not have exercised as rigorously as required and consequently, not show an increased VO_{2peak} associated with HIIT (Gibala & Mcgee, 2008).

4.2 The Effects of a 14-Week Exercise Intervention on Pain Perception and Mechanical Detection Threshold

In my study, baseline-assessed pain thresholds (thermal-, mechanical-, pressure pain threshold) measured in the left hand, and perception of pain during ischaemia measured in the right arm, were not different between healthy-weight and overweight women. According to an extensive literature review, only one other study (Tashani *et al.*, 2017) has compared pain perception of healthy-weight and overweight participants. Tashani *et al.* (2017) reported no differences in pain perception (heat-, cold- and pressure pain threshold, heat- and cold pain tolerance, cold pain ratings) measured in different anatomical areas (dorsal thumb web, suprailiac, hand) between overweight and healthy-weight men and women (Tashani *et al.*, 2017). Therefore, perhaps mechanisms responsible for the differences in pain perception between healthy-weight and obese individuals, such as systemic inflammation (Maury *et al.*, 2007) and increased leptin (such as hypothesised in section 1.1.1), may not be present (or less present to have an effect), in an overweight population. However, the study sample of overweight women in the current study included obese women; in fact, the BMI of the exercising and non-exercising overweight women averaged at 33- and 30.7 kg/m^2. The results of this study are contrary to those who reported decreased pressure pain thresholds (McKendall & Haier, 1983) and increased cold- and heat pain thresholds (Miscio *et al.*, 2005; Price *et al.*, 2013) in obese men and women compared to

healthy-weight controls, measured on the fingertips. The current study is in agreement with those who reported no differences in cold- and heat pain thresholds in obese men and women compared to healthy-weight controls, measured on the abdomen (Price *et al.*, 2013). The results of this study and those of McKendall & Haier (1983) and Price *et al.* (2013) support the Lep-R desensitisation hypothesis that areas of high subcutaneous fat, such as the abdomen, may have Lep-R desensitisation and therefore reduced pain thresholds, while areas with similar subcutaneous fat, such as the fingers and hands, may show no change or decreased pain thresholds. Nevertheless, more research is required to confirm the Lep-R desensitisation hypothesis and asertain whether pain perception is different in healthy-weight and overweight individuals.

No changes in pain perception were observed in heat-, mechanical-, pressure- and ischaemic pain from baseline to post-exercise intervention in the healthy-weight and overweight women. However, in direct contrast to my hypothesis, after the 14-week HIIT intervention, cold pain hyperalgesia (increased sensitivity to cold pain) was observed in both exercising and non-exercising overweight women.

This study is the first to use thermal (cold and heat) pain sensitivity as a method of experimental pain with HIIT as an exercise intervention to assess any changes in pain perception after regular exercise. Studies that have used experimental thermal (heat- and cold) pain to assess the perception of pain before and after exercise have only used acute exercise, none of which included HIIT, and have yielded inconsistent results; varying from no effect (Kemppainen *et al.*, 1998), EIH (Vierck *et al.*, 2001; Staud *et al.*, 2005) and hyperalgesia (Cook *et al.*, 2010). The inconsistent results have been attributed to differences in population groups. More specifically, studies reporting no effects of exercise on thermal pain were done in pain-free participants (Kemppainen *et al.*, 1998; Sternberg *et al.*, 2001; Vierck *et al.*, 2001; Ruble *et al.*, 2005; Staud *et al.*, 2005), while patients with chronic pain have shown post-exercise thermal pain hyperalgesia (Vierck *et al.*, 2001; Staud *et al.*, 2005; Cook *et al.*, 2010). Similarly, in line with the findings of other acute exercise studies (Vierck *et al.*, 2001; Staud *et al.*, 2005; Cook *et al.*, 2010), in the current study cold pain hyperalgesia following the 14-week HIIT intervention was observed in overweight women, who had a 60% prevalence of chronic pain. Therefore, it may be suggested that the effects of acute exercise, more specifically cold pain hyperalgesia, seen in individuals

with chronic pain may be present after regular exercise too, for as long as 48 hours after the cessation of the exercise intervention.

Inflammation associated with chronic pain, exacerbated by regular high-intensity exercise, may mediate cold pain hyperalgesia seen in the current study. Indeed, molecular studies have shown that inflammation may cause cold pain hyperalgesia (Obata *et al.*, 2005; Kwan & Corey, 2009; Camino *et al.*, 2010). However, this does not explain the presence of cold pain hyperalgesia in the overweight non-exercising women. A possible explanation includes the anticipation of pain at the 14-week assessment intensifying sensitivity to pain through the activation of brain regions, including the anterior cingulate cortex, parietal operculum and posterior insula, all of which are responsible for the modulation of pain (Sawamoto *et al.*, 2000). Another study has shown that the anticipation of pain increases the activity of the hypothalamic-pituitary-adrenal axis and the subsequent release of cortisol which may intensify sensitivity to pain (Benedetti *et al.*, 2006). Therefore, perhaps the increased sensitivity to cold pain post-intervention may be attributed to the anticipation of pain in the non-exercising overweight women. Another explanation is that, since our study design entailed pain assessment before and after an exercise intervention, it did not allow for the randomisation of the order of pain tests (i.e., before and after the intervention). Therefore, it may be that the non-exercising overweight women had an increased pain perception the second time they were exposed to the pain (i.e., an order effect) possibly due to the anticipation of pain (Sawamoto *et al.*, 2000; Benedetti *et al.*, 2006).

In contrast, no heat pain hyperalgesia was observed in the overweight, nor the healthy-weight women after the 14-week HIIT intervention. Studies reporting heat pain hyperalgesia after acute exercise in obese men (Cook *et al.*, 2010) and women (unknown BMI) (Staud *et al.*, 2005) have specifically assessed heat pain ratings, and not heat pain thresholds. Indeed, in accordance with the results from my study, when heat pain thresholds were assessed following an acute 30-minute treadmill MICT intervention in healthy-weight men and women, no heat pain hyperalgesia was observed (Ruble *et al.*, 2005). Therefore, conflicting results may be attributed to the mechanism by which thermal pain outcomes are measured; however, more research on the effects of regular exercise on heat pain threshold and heat pain ratings is required to confirm this theory.

No exercise-induced changes in pressure pain thresholds in the healthy-weight and overweight women were found in the current study after the 14-week HIIT intervention. Only two studies have used pressure pain as a means of assessing experimental pain sensitivity before and after a HIIT intervention stretching over 6- to 16 weeks (Hakansson *et al.*, 2018; Mijwel *et al.*, 2018). In agreement with the current study, Hakansson *et al.* (2018) reported no change in pressure pain threshold in overweight men after a 6-week cycling HIIT intervention. In contrast, pressure pain EIH was observed in healthy weight women with cancer after a 16-week cycling HIIT intervention (Mijwel *et al.*, 2018). The inconsistent results in pressure pain amongst studies that have assessed HIIT may be attributed to differences in methods. More specifically, Mijwel *et al.* (2018) used a HIIT intervention in conjunction with resistance exercise. In addition to a 3×3 minutes cycling HIIT intervention, participants were required to partake in weight lifting (2-3 sessions with 8-12 repetitions) (Mijwel *et al.*, 2018). Therefore, it is unclear whether the HIIT, the resistance exercise or the combination of both interventions were responsible for the pressure pain EIH reported by Mijwel *et al.* (2018). Moreover, the author suggested that the pressure pain EIH may be attributed to the taxane-based chemotherapy, whereby taxanes have been reported to increase numbness and reduce vibratory perception which may appear as EIH (Mijwel *et al.*, 2018).

Mechanical pain thresholds also did not change from baseline to post-exercise in both the healthy-weight and overweight women. This is the first study to assess mechanical pain thresholds before and after an exercise intervention, and hence, it is unclear whether it is the HIIT intervention, or the exercise in general, that does not change the perception of experimental mechanical pain in healthy-weight and overweight women. Since mechanical-, heat- and pressure pain stimuli transduce pain via common nociceptors, such as mechano-heat TRPV1 nociceptors (Dubin & Patapoutian, 2010), it is possible that mechanical pain thresholds may follow the same pattern as seen with heat pain and pressure pain threshold, particularly since no changes were obeserved in pressure- and heat pain sensitivity after exercise in the current study and in others (Ruble *et al.*, 2005; Hakansson *et al.*, 2018). Nevertheless, both pressure and mechanical pain thresholds were assessed as each method assesses pain perception at different tissue depths. For example, noxious pricking, the method used to assess mechanical pain

thresholds, assesses pain perception of the skin (epidermis and dermis), whereas pressure pain threshold assesses pain perception of deep tissue, such as muscle (Fein, 2012).

Similarly, experimental ischaemic pain ratings, which assesses deep tissue pain, were not different in healthy-weight and overweight women, from baseline to post-intervention. Only one study assessing the effects of a regular HIIT intervention on pain perception has assessed ischaemic pain (O'Leary *et al.*, 2017). More specifically, ischaemic pain tolerance, but not ischaemic pain ratings, was improved in overweight participants after a 6-week cycling HIIT intervention. Although an increased post-exercise pain tolerance may be indicative of EIH, no change in ischaemic pain ratings, such as seen in the current study and the study of O'Leary *et al.* (2017), may suggest that EIH might not be responsible for the increased pain tolerance seen in O'Leary *et al.* (2017). It has previously been suggested that the increased pain tolerance may be attributed to the adaptation of nociceptive afferents to exercise-induced noxious metabolic accumulations, similar to the noxious metabolic accumulations during ischaemia (Jones *et al.*, 2014).

Lastly, mechanical detection thresholds were not affected by the 14-week HIIT intervention in both the healthy-weight and overweight women in this study. This finding confirms that the effects of the HIIT intervention did not extend to the general somatosensory system, but rather specifically targeted the nociceptive (pain) system, with particular reference to the overweight women and cold pain.

4.3 The Effects of a 14-Week Exercise Intervention on Sleep Quality

In support of my hypothesis, sleep quality was improved in overweight women after a 14-week HIIT intervention. These results support those of two other studies investigating the effects of a regular running HIIT intervention, spanning 1- to 12 weeks, on sleep quality in obese participants (Karlsen *et al.*, 2017*b*; Irandoust & Taheri, 2018). More specifically, improved sleep quality, assessed by the apnoea hypopnoea index and Epworth sleepiness scale, was reported in obese patients with obstructive sleep apnoea after a 16-minute HIIT intervention spanning over 12 weeks (Karlsen *et al.*, 2017*b*). Similarly, after a short 1-week HIIT intervention, Irandoust & Taheri (2018) reported improved sleep quality, assessed using actigraphy, in obese women with

poor sleep quality at baseline (PSQI score > 11). As such, both these studies investigated obese patients with sleep disorders or with high global PSQI scores (Karlsen *et al.*, 2017*b*; Irandoust & Taheri, 2018). In the current study, overweight exercising women also had poor sleep quality at baseline (global PSQI score = 8 ± 1.9). Together, this study, and other studies assessing the impact of HIIT on sleep quality (Karlsen *et al.*, 2017*b*; Irandoust & Taheri, 2018), support the notion that exercise-induced sleep improvements are prevalent in patients who have poor sleep quality at baseline (Chennaoui *et al.*, 2015).

Similarly, studies support MICT-induced sleep improvements in individuals with poor sleep quality using regular MICT interventions (7- to 24 weeks) with durations ranging between 25-60 minutes (King *et al.*, 1997; Singh *et al.*, 1997; Sherrill *et al.*, 1998; Esteves *et al.*, 2009; Reid *et al.*, 2010; Hosseini *et al.*, 2011; Richards *et al.*, 2011). Here, I show that, a 14-week HIIT intervention of only 11 minutes is effective for improving sleep quality of participants with poor sleep quality, and hence, HIIT may serve as a more time-efficient intervention to improve sleep quality in overweight women with poor sleep quality, compared with MICT.

Moreover, the current study has shown that, each overweight woman following the 14-week HIIT intervention may report an improvement in global subjective sleep quality, compared to following no intervention as seen from the NNT of 1. More specifically, one in every two women following the HIIT intervention will rate their sleep quality better if they follow the 14-week HIIT intervention, compared to not following the intervention, according to the NNT. This study is the first to calculate an NNT for assessing the clinical impact of a HIIT intervention. The NNT strengthens the observation that HIIT improves sleep quality in overweight women.

Although an improvement in sleep quality of overweight women after the 14-week HIIT intervention was shown, no changes in sleep onset latency, sleep duration, sleep efficiency, use of sleep medication, sleep disturbance and daytime dysfunction was noted in these women after the 14-week intervention. The absence of exercise-induced improvements in sleep onset latency, sleep duration and sleep efficiency contradict the findings of a meta-analytic review in which a small-to-moderate effect of regular exercise on these specific PSQI scores was shown (Kredlow *et al.*, 2015). This meta-analytic review included study populations with ages ranging from young adults to elderly, with and without sleep disorders, as well as differing exercise modalities. The authors reported that too few regular-exercise studies exist to assess each

variable individually (Kredlow *et al.*, 2015). Nevertheless, an older review reported that exercise-induced sleep improvements after regular exercise are mediated by age, health status and exercise modality (Driver & Taylor, 2000). More specifically, exercise-induced sleep improvements after aerobic exercise are more prevalent in elderly populations and in populations with sleep complaints (Driver & Taylor, 2000). Therefore, the results of the meta-analytic review (Kredlow *et al.*, 2015) may have been affected by these confounding variables. In addition, exercise-induced improvements in PSQI component scores are more prevalent in patients with insomnia than patients with other sleep complaints (Banno *et al.*, 2018).

Importantly, improvements in PSQI sleep quality scores, as reported in the current study after the 14-week HIIT intervention in the overweight women, has been identified as the greatest predictor of quality of life (Zeitlhofer *et al.*, 2000). Therefore, although no improvements were observed in other PSQI scores - likely due to the limited sample size - the 14-week HIIT intervention improved sleep quality and, by inference (although not assessed), may have improved quality of life in overweight women with poor sleep quality.

This study did not show the same exercise-induced sleep quality improvement in the healthy-weight women, as hypothesised. Similarly, no exercise-induced sleep improvements were reported in healthy-weight men and women after an *acute* HIIT intervention (Passos *et al.*, 2010; Vitale *et al.*, 2017). According to systematic reviews, exercise-induced improvements in sleep quality are not common in healthy, good-sleeping participants (Youngstedt *et al.*, 1997; Driver & Taylor, 2000; Chennaoui *et al.*, 2015). Therefore, the absence of exercise-induced sleep improvements seen in the healthy-weight women from the current study, may be attributed to the group having good sleep quality at baseline (baseline global PSQI score = 4.9 ± 1.8), and hence, support the notion that there may have been little room for improvement (Chennaoui *et al.*, 2015).

4.4 Correlation between Baseline Waist Circumference, Body Mass Index and Pain Perception and Sleep Quality

The results of my study showed that waist circumference and BMI was not associated with cold-, pressure-, mechanical- and ischaemic pain at baseline. These results contrast the findings of

another study which showed an association between BMI and pressure pain thresholds measured on the thenar muscle of 74 women (Tashani *et al.*, 2017). Discrepancies in results may be attributed to the smaller sample size of the current study and the study sample's distribution in various BMI categories, where Tashani *et al.* (2017) used 25, 24 and 25 participants in the healthy-weight, overweight and obese categories, respectively, while in the current study there were 16, 9 and 11 participants in the healthy-weight, overweight and obese categories, respectively. It is possible that a greater sample size with an even distribution among the BMI categories may have yielded a stronger relationship between BMI and pressure pain thresholds in the current study.

Nevertheless, the current study showed an association between increased heat pain thresholds (reduced heat pain sensitivity) and increased BMI, but not waist circumference, suggesting that BMI, as opposed to central adiposity, is associated with heat pain perception in an obese population. These results are in agreement with another study which has showed that obesity is associated with increased heat pain threshold, and thus reduced heat pain sensitivity, compared to healthy-weight controls (Miscio *et al.*, 2005). It has been suggested by Miscio *et al.* (2005) that reduced heat pain sensitivity in obesity is an indication of early peripheral neuropathy mediated by obesity-related hyperinsulinemia, as a results of action potential disruptions (Brismar *et al.*, 1987; Brismar, 1993). More research is required to substantiate the notion that obesity-related hyperinsulinemia mediates increased heat pain threshold.

Similar to other studies, the current study showed an association between baseline poor sleep quality, reduced sleep duration and increased waist circumference, but not BMI (Grunstein *et al.*, 1993; Davidson & Patel, 2008; Stranges *et al.*, 2008; Ford *et al.*, 2014). Studies have shown increased waist circumference, but not BMI, to be strongly associated with the presence of sleep disordered breathing, such as sleep apnoea, in men and women (Grunstein *et al.*, 1993; Davidson & Patel, 2008). Moreover, two studies reported an inverse relationship between waist circumference and sleep duration, whereby sleep duration is decreased with increased waist circumference (Stranges *et al.*, 2008; Ford *et al.*, 2014).

Increased adipose tissue has been implicated in the prevalence of poor sleep quality in overweight and obese individuals. In particular, the release of increased IL-6 and TNF-α concentrations from the increased adipose tissue, such as seen in overweight and obesity, have

been implicated in poor sleep quality (Vgontzas *et al.*, 1997; Obal & Krueger, 2003) and the pathogenesis of regular sleep disorders (Vgontzas *et al.*, 1997; Liu *et al.*, 2000; Mills *et al.*, 2007). Similarly, the current dissertation showed that increased waist circumference and, by inference, central adiposity, is associated with both poor sleep quality and reduced sleep durations.

4.5 Limitations

The sample size of the current dissertation, although adequate for detecting differences in sleep quality, was likely inadequate to detect differences in pain data. Pain perception has large inter- and intra-person variation (Oono *et al.*, 2011). Thus, a larger sample size, with greater statistical power, may have been able to account for the inter- and intra-person variability in pain perception. Studies that have assessed the effects of HIIT on pain perception, and did not observe changes in pain perception, used smaller sample sizes to the current dissertation (n = 20) (O'Leary *et al.*, 2017, n = 10; Hakansson *et al.*, 2018, n = 16). In contrast, Mijwel *et al.* (2018) used a study sample between 72 and 74 women per HIIT intervention, and reported pressure pain EIH. For the current study, a larger sample size will also strengthen the statistical outcomes of the hypotheses, especially for those which, although declared as statistically significant, leans towards the significance thresholds. In addition to a larger sample size, stratifying the sample into healthy-weight, overweight and obese groups, as opposed to incorporating obese individuals into overweight groups, may have yielded different pain perception results and possibly stronger correlations between anthropometry and pain perception; however, this could not be done with the current sample size. To test the hypotheses of the study, the majority of the analyses involved multiple comparisons which draws caution to the interpretation of the results, as multiple comparisons can yield false positives and/or negatives. To minimise the effect of multiple comparisons, the Bonferroni and Tukey correction with adjusted p-values that correct for multiple comparisons were used for analyses.

Although some promising correlations were observed between BMI, waist circumference, heat pain threshold and sleep components, these relationships are potentially much more complex, such as described in Section 1.1. Therefore, a multi-factorial regression model including

variables such as sleep, pain perception and cytokine concentrations, may have produced a more in-depth understanding of the complex relationship between pain, sleep and anthropometry. Covariates, such as diabetes and occupation, were not assessed and, consequently, not adjusted for in the current dissertation. Adjusting for diabetes may have altered the pain results, as diabetes is associated with the occurrence of neuropathy and diminished conduction velocity of nerve fibres (Chiles *et al.*, 2014), consequently affecting the perception of pain. Adjusting for occupation holds importance for sleep research as changes in work hours or transitions from day- to night shifts affects sleep quality (Lim *et al.*, 2018).

The current dissertation did not require participants to document, or limit, their caloric intake. Therefore, it is unclear whether the absence of improved body fat percentage, or any anthropometric measurements, may have been due to a change in dietary intake (quantity and quality) to compensate for the increased energy expenditure following the exercise intervention; a phenomenon that is commonly observed with increased physical activity (Poehlman *et al.*, 1990). In addition, body fat percentages were calculated using skin-fold measurements. Assessing body fat percentages with body scans and air-displacement techniques may have captured minor changes, which may not be detected with skin-fold measurements, however these techniques were not available for the current study.

Furthermore, a HIIT intervention with a period longer than 14 weeks may have yielded different results. Studies assessing the effects of HIIT on pain perception, including the current study, in which no changes in pain perception were reported used interventions between 6 and 14 weeks (O'Leary *et al.*, 2017; Hakansson *et al.*, 2018). In the study of Mijwel *et al.* (2018), the HIIT intervention took place over 16 weeks after which EIH was reported. As such, a longer intervention, ideally with dietary control, could have possibly yielded anthropometric changes, such as body fat percentage (Trapp *et al.*, 2008), which may have yielded changes in pain perception results and more extensive positive effects on sleep.

Assessing sleep using objective measures, such as actigraphy or PSG recordings, would have complimented my findings of an improved subjective sleep quality in overweight women after the 14-week exercise intervention. PSG could have revealed information, and possibly correlations between sleep composition, including individual sleep stages, and various anthropometric variables. In addition, our study did not assess sleep quality for a period after

participants abstained from the HIIIT intervention; therefore, it is unclear how long the exercise-induced sleep improvements lasted in the overweight women.

Because the aim of the study was to specifically assess the efficacy of a home-based intervention, the study was reliant on participants' honesty, diligence, and accurate recollection. I therefore recognise that compliance to one, or all of these, are limitations to the current study. Participants may not have been completely honest about their compliance to their respective group intervention, which may influence the conclusions deducted from the results of the study. Nevertheless, participants were encouraged to be truthful in reporting their activity even if it violates the instructions for their respective group intervention. As such, some participants did indeed report not complying with their respective group intervention during certain days, such as participating in exercise whilst in the non-exercising group or exercising less than required while in the exercising group, hence the 82% compliance.

Lastly, the current study did not measure process evaluation of the HIIT intervention. Process evaluation data would have attributed insightful information about the 14-week HIIT intervention and how the data have been gathered from the participants, to identify limitations to the study that could have been addressed before or during the study, as well as limitations that could be addressed in future studies.

4.6 Future Studies

Apart from an improved waist circumference in overweight women, the 14-week HIIT intervention did not change any other anthropometric measures in the healthy-weight and overweight women in this study. It has been suggested that HIIT interventions with the intermittent exercise bouts longer than two minutes may be required to reduce body mass of healthy-weight and overweight women. Future studies could assess a regular HIIT intervention of different intermittent exercise bout durations (< 2 minutes, versus > 2 minutes) to determine whether the duration is associated with a change in anthropometry, such as body mass. Additionally, future studies should use more accurate techniques to measures body composition, such as the dual energy x-ray absorptiometry to assess body fat percentage (Clasey *et al.*, 1997), as well as require participants to document dietary intake.

Before the 14-week intervention, baseline measures of pain perception were not different between the healthy-weight and overweight women, suggesting that the perception of pain in these two groups of women is similar. In the present sample of women, the 14-week HIIT intervention did not alter the pain thresholds to heat, mechanical and pressure stimuli, nor did it alter the perception of ischaemic pain. Only cold pain threshold was altered by the 14-week HIIT intervention in both overweight groups (exercising and non-exercising women). An extrapolation of this supports the hypothesis that exercise may induce thermal pain hyperalgesia in populations with chronic pain, since 60% of the overweight women reported having chronic pain. However, this does not explain why the overweight non-exercising women also experienced hyperalgesia to cold, and this finding is worthy of further exploration. Possible paths to explore include the anticipation of painful stimuli, which has been shown to enhance pain sensitivity (Sawamoto *et al.*, 2000) through the increased activity of the hypothalamic-pituitary-adrenal axis (Benedetti *et al.*, 2006). As such, future studies could measure activity of the hypothalamic-pituitary-adrenal axis, through plasma concentrations of cortisol, before experimental pain assessments to correct for anxiety-induced hyperalgesia (Benedetti *et al.*, 2006).

More studies, with larger sample sizes, assessing the full range of pain parameters, such as the QST, are required to fully understand the effects of HIIT on pain perception. This is the first study to assess all pain parameters together and the first to assess thermal and mechanical pain after a regular HIIT intervention. Additionally, more research assessing mechanical detection threshold before and after a regular exercise intervention is required to determine if and how exercise affects the sensory detection pathways.

The current study set out to test the effect of a 14-week HIIT intervention; therefore, testing the long-term health benefits of a long-term HIIT intervention was beyond the scope of the study. The health-benefits of a long-term HIIT intervention (≥ 24 weeks) will depend on various factors including attrition, adherence to the specified intensity and volume of the exercise as well as maintaining a good form and/or posture while performing the exercise. Nevertheless, potential long-term benefits may include sustained or greater improvements in sleep quality in overweight women, improvements in quality of life in overweight women (as discussed in section 4.3), possible improvements in pain thresholds and improved aerobic capacity in both healthy weight and overweight women which may reduce the risk for metabolic disease (Tjonna et al., 2008). As

such, future studies should assess the efficacy of a long-term HIIT intervention in light of attrition rates and adherence to the intervention and the potential health benefits a long-term HIIT intervention may hold. Additionally, these studies should include process evaluation data for identifying the efficacy for implementing such long-term HIIT interventions.

The 14-week HIIT intervention improved subjective sleep quality of overweight women. Importantly, the results indicate that a regular HIIT intervention may be a more time-efficient intervention for improving sleeping quality compared to ≥ 30 minutes of moderate-intensity continuous training. Moreover, the results support the notion that exercise-induced sleep improvements are more prevalent in populations with poor sleep quality than healthy, good-sleeping populations. Future studies should assess sleep quality for a pre-determined period post-exercise to determine whether exercise-induced sleep improvements are preserved in participants. Extending the research in this area should include objective measures of sleep, preferably the gold standard polysomnography, with an NNT to compliment the findings of improved subjective sleep quality in overweight women.

4.7 Conclusion and Implications of the Current Study

The 14-week HIIT intervention was effective at improving waist circumference and sleep quality in overweight women, with an NNT confirming the clinical relevance of HIIT for improving sleep quality. Waist circumference is an indirect measure of central obesity, which, in turn, is associated with various comorbidities, such as metabolic syndrome (Wei *et al.*, 2006), and reduced sleep quality (Theorell-Haglöw *et al.*, 2010) and sleep disorders (Davidson & Patel, 2008). The association between central obesity and comorbidities may be mediated by the secretion of substances such as adipokines (Maury *et al.*, 2007). Therefore, reductions in waist circumference reported by the current study may hold clinical importance with regards to improving comorbidities associated with central obesity, such as reduced sleep quality.

Further, improved sleep quality is associated with improved quality of life, more specifically improved occupational functioning, physical health and mental health (Zeitlhofer *et al.*, 2000). Remarkably, exercise-induced improvements in sleep quality has been reported to have the same effect size as the use of pharmacological agents for the improvement of poor sleep quality (Smith

et al., 2002; Kredlow *et al.*, 2015). Therefore, by inference, a 14-week HIIT intervention may hold similar sleep-improving advantages, without the adverse effects associated with pharmacological agents.

In conclusion, the current dissertation has shown that HIIT is an effective home-based, non-pharmacological intervention for improving subjective sleep quality in overweight women. However, the 14-week HIIT intervention may not be effective for improving pain in healthy weight and overweight women. Additionally, increased BMI and waist circumference may mediate increased pain sensitivity and poor sleep quality, respectively, in South African women.

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6. APPENDIX

Appendix I: Ethics clearance certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr Rebecca Meiring et al

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M180253

NAME: (Principal Investigator)	Dr Rebecca Meiring et al
DEPARTMENT:	School of Physiology Movement Physiology Research Laboratory
PROJECT TITLE:	The effect of high intensity intermittent training on body composition and cardiometabolic health in healthy and overweight/obese women
DATE CONSIDERED:	23/02/2018
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	
APPROVED BY:	Prof C Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	02/05/2018

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary in Room 301, Third floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in February and will therefore be due in the month of February each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

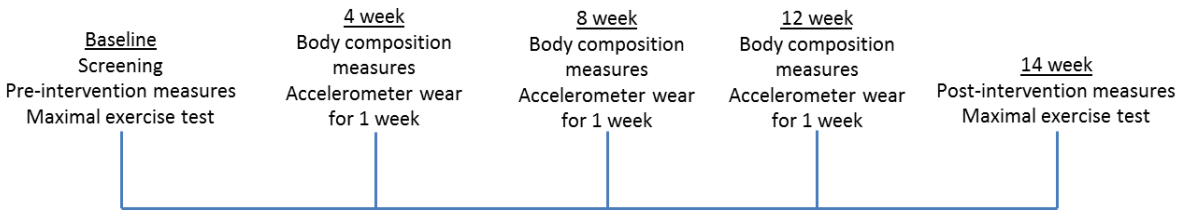
02/052018
Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix II: Information sheet with an overview of the study

Good day.

We are Aletta and Emmanuel. We are researchers in the School of Physiology and are interested in understanding the effects of different types of exercise on health. We, along with our co-workers (Rebecca, Chloe and Janine) from Wits University, would like to invite you to take part in our study. We are interested in looking at the effects of taking part in a certain type of exercise on various aspects of your health including your heart health and your body weight. The figure below summarises the commitment required from you for the study. At the first visit the study we would like you to fill out two questionnaires. One questionnaire asks about your health and exercise capacity in general and the other questionnaire asks about your sleep. The questionnaires will take approximately 20 minutes to complete. A researcher will be able to assist you should you have any questions. At the first visit of the study we will also need to take measurements of your height and weight and a measure of the amount of body fat you have. We would also appreciate you providing a 15 ml blood sample that will need to be drawn from the vein in your arm as well as a small drop of blood from a finger prick. At the end of the study we will repeat some of the measures taken at the first visit. All measurements will be done at the School of Physiology, 6th floor WITS medical school.



What would we like you to do?

This study will look at the effects of high intensity exercise and its effects on heart health and sensory perception. In this study we would like you to participate either by undertaking a 14 week exercise program or by continuing with your normal exercise routine for 14 weeks (called a control group). The group in which we would like you to participate in will be assigned in a random way which will be independently determined.

We would like you to come in to the lab on a few occasions; before and after the 14 weeks for some measurements as well as at weeks 4, 8 and 12 to be weighed and receive an activity monitor. The measurements we need to take before and after the 14 weeks will be measures of how much you weigh and your height, heart health and we would like you to give us a 15ml blood sample (about a tablespoon). The blood sample will be drawn from the vein in your arm and a drop of blood will also need to be taken by finger prick. You may experience slight pain with the blood sampling. The blood sample will be used to measure your cholesterol and blood sugar levels and other biomarkers of your cardiovascular and metabolic health. We will then take some measures of your heart and blood vessel function and sensory perception. In order to evaluate if your blood vessels are stiffened, a procedure called 'applanation tonometry' will be performed. This non-invasive painless procedure involves applying a probe over the area of the main artery in your wrist and groin. This investigation would take 5-10 minutes. In order to determine the size and the function of your heart an echocardiogram (cardiac ultrasound) will be used. Echocardiography is also non-invasive and involves a transducer (probe) with gel being placed on your chest, in the area of your heart, and is not painful. This procedure is similar to an ultrasound done during pregnancy, and will not harm you in any way. This investigation will take approximately 30 minutes. Sensory perception testing will assess your responses to changes in temperature, touch, vibration and pressure. These tests are all performed by placing the various testing devices on the surface of the hand and are designed to detect when you **first feel** pain, pressure, touch or change in temperature. Some of these measures may be slightly painful however the test ends immediately after you start to feel a pain-like sensation. You will also be asked to perform the sub-maximal effort tourniquet test. A blood pressure cuff will be placed on your upper-arm and pumped up to decrease blood flow to your forearm. Once the cuff is inflated, you will be asked to perform hand-grip exercises which are similar to squeezing a soft tennis ball. The exercises will last for approximately 2 minutes. Once you have completed the hand-grip exercises the cuff will remain inflated for 10 minutes during which you will be asked to rate your pain on a scale. The cuff will then be deflated. The pain you will feel will range from mild to moderate and will last for a maximum of 10 minutes. The procedure will not cause any damage to your forearm.

We would then like you to perform a walking test on a treadmill that will help us determine the specific intensity of exercise that we would like you to do at home if you have been assigned to the 14 week exercise program group. During this test we will need you to wear a face mask that is comfortable but will feel unusual to you.

This is so we can measure how much oxygen your body is using while you exercise. This test will make you tired but you are allowed to stop the test whenever you feel you cannot carry on.

Once you are finished with these tests we will then explain the exercise program to you before you go home.

The exercise programme is a high intensity exercise programme that will need to be done for 10 minutes a day, twice a day, three times a week. That means that each week you will be exercising for a total of 60 minutes a week. This exercise programme will need to be performed for 14 weeks. We will give you a diary to record the number of times you perform a full session of the exercise program. Every 4 weeks we would like to monitor your activity while performing the exercise program using a small device called an accelerometer. An accelerometer is the size of a bottle top and fits on a waist band around your waist. This device will need to be worn for seven days. We will arrange to drop off and collect (via courier) the device with you on those weeks. During the weeks you are wearing the activity monitor we will also ask you to keep a sleep diary. In this sleep diary we will ask you to record bed time, sleep onset latency, waking time, subjective sleep quality and daytime sleepiness as well as some general questions about your sleep.

If you are allocated to the control group, you will be asked to not change your routine for the next 14 weeks and you will be asked to not undertake any new exercise programmes. If you are allocated to the control group and once you have completed your 14 weeks, we will give you the exercise programme for you to do at home at your leisure.

In summary the things we require from you:

At the start of the study:

- Complete questionnaires
- Measures of body composition, blood sample, heart assessment, sensory perception testing
- Maximal voluntary exercise test
- Measure of physical activity

During the study:

- Measures of physical activity and body composition every 4 weeks
- Exercise diary and sleep diary for 1 week every 4 weeks

After the study:

- Complete questionnaires
- Measures of body composition, blood sample, heart assessment, sensory perception testing
- Maximal voluntary exercise test
- Measure of physical activity

All procedures will be explained to you and you can ask as many questions as you like if you do not understand any part of the study. All information that is collected will remain anonymous to anyone who is not associated with the study. All data obtained will be kept strictly confidential. If you experience any adverse events or are found to have abnormal blood tests, specialists within the School of Physiology are able to refer you to the relevant healthcare practitioner for further follow up. We would like to emphasize that participation is completely voluntary and if you do not want to continue with the study **you can withdraw at any time without prejudice.** The data will be made available to you should you be interested in the outcomes of the study.

Thank you for considering participation in this study. Please read the information sheet carefully before signing the consent form*. If you have any queries, please contact myself Aletta. Tel: 011 7172254, Email: Aletta.Millen@wits.ac.za OR Emmanuel, Tel: 081 523 7799, Email: Emmanuel.Frimpong@wits.ac.za.

***If you have any doubts to your rights as a participant please feel free to contact** Mr Rhulani Mkansi Rhulani.Mkansi@wits.ac.za or Ms Zanele Ndlovu zanele.ndlovu@wits.ac.za – 011 717 1252/2700/1234/2656**, Medical School, Parktown, Phillip Tobias Building, 2nd Floor, Cnr York Road and Princess of Wales Terrace, Mon-Fri 08h00-17h00. Chair of the Human Research Ethics Committee.**

Appendix III: High-intensity interval training intervention

High knees	30 seconds
Alternating side backward lunge (like you are skiing)	30 seconds
Squat jumps (jump and squat)	30 seconds
Inch worm (crawl and plank)	30 seconds
Active rest (walk around for 1 minute)	
Sumo Squat (jump and wide leg squat)	30 seconds
Burpees	30 seconds
Jump to the side lunge	30 seconds
Mountain climbers (plank)	30 seconds
Active rest 1 minute	
High knees	30 seconds
Alternating side backward lunge (like you are skiing)	30 seconds
Squat jumps (jump and squat)	30 seconds
Inch worm (crawl and plank)	30 seconds
Active rest 1 minute	
Sumo Squat (jump and wide leg squat)	30 seconds
Burpees	30 seconds
Jump to the side lunge	30 seconds
Mountain climbers (plank)	30 seconds
Active rest – well done!	

Appendix IV: Plagiarism report

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3	Black, Christopher D., and Kori E. Pickowitz. "Day-to-day reliability of pressure pain threshold and pain ratings in college-aged men :", International Journal of Rehabilitation Research, 2015. Publication	<1%