

The development of an exercise intervention framework as a modality of treatment for individuals with obstructive sleep apnoea, in the South African public healthcare setting

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LIST OF ABBREVIATIONS

1RM: One-repetition maximum

ACSM: American Council of Sports Medicine

AHI: Apnoea hypopnea index

BMI: Body mass index

BP: Blood pressure

CMD: Cardiometabolic disease

CON: Control

CPAP: Continuous positive airway pressure

CVD: Cardiovascular disease

EDS: Excessive daytime sleepiness

EE: Energy expenditure

ESS: Epworth Sleepiness Scale

HDL: High-density lipoprotein

HR: Heart rate

HRR: Heart rate reserve

IL-6: Interleukin-6

MRC: Medical Research Council

LDL: Low-density lipoprotein

NREM: Non-rapid eye movement

ODI: Oxygen desaturation index

OSA: Obstructive sleep apnoea

PA: Physical activity

PSG: Polysomnography

QOL: Quality of life

RCT: Randomised control trial

REM: Rapid eye movement

SES: Socioeconomic status

T2DM: Type 2 diabetes mellitus

VE: Peak ventilation

VE/VCO₂: Minute ventilation/volume of carbon dioxide produced

VO₂max: Maximum oxygen uptake (L/min)

ABSTRACT

Introduction: Obstructive sleep apnoea (OSA) is described as a breathing-related sleep disorder wherein your ventilation is impaired during sleep, due to the narrowing and collapse of the upper airway. Untreated OSA has been shown to increase the number of severe cardiovascular and cerebrovascular events. Common treatment modalities for OSA, including surgical intervention and continuous positive airway pressure therapy are effective but remain extremely expensive. It is thus often inaccessible to those in a low-income, under-resourced setting, or those without access to healthcare, as is the case for the majority of South Africans. Since addressing weight loss is a key component of OSA treatment, exercise may provide the benefits of addressing both weight loss and inflammation in OSA patients, as well as lowering the risk of cardiovascular disease, depression, and comorbidities that arise from obesity. **Aims:** The aims of this study were to understand the nature of, and perception to, current physical activity (PA) habits as well as barriers to exercise, faced by individuals with obstructive sleep apnoea (OSA group) compared to a control group of individuals without OSA (CON group). This information was then used to design an exercise intervention framework for OSA patients which can be implemented in an under-resourced setting, such as in the public healthcare system in South Africa. **Methods:** This is a secondary analysis of data already collected as part of a larger study investigating “Physical activity and sedentary behavior among patients with obstructive sleep apnoea in South Africa” (HREC Ref: 142/2021). The parent observational study made use of custom and validated questionnaires answered by adults diagnosed with moderate to severe OSA and control participants with no OSA. Participants were asked to report on current and past exercise habits, perceptions, enablers, and barriers to PA, as well as preferred modes of exercise, which were further analyzed. **Results:** A total of thirty-seven adults were included in the current study; eighteen of whom had been diagnosed with OSA, matched with nineteen CON adults for age, BMI, neck circumference, waist circumference, and blood pressure (all $p > 0.050$). Self-reported current participation in PA was lower in the OSA group (61%) compared to the CON group (74%), although not significantly different ($p = 0.410$), with lower levels of PA between the two groups reported as being due to time constraints, dark/unsafe environment, laziness, covid restrictions, a lack of interest, motivation, and illness/injury/surgery within the OSA group specifically, There was a high presence of structural pain within the OSA group (83%) compared to the CON group (58%), although not significantly different (0.091), which was aggravated by PA (33% and 36% respectively). Frequency of PA was most commonly recorded as four to seven days per week by both the CON and OSA group ($p = 0.975$, with a self-reported medium intensity ranging between 4-7 out of 10 ($p = 0.281$) based on a subjectively designed 10-point scale (1: very low intensity, 10: very high intensity). Walking was the preferred form of PA within the OSA group (72%), as well as within the CON group (63%) ($p = 0.556$), and both groups identified the ‘lack of motivation’ as a barrier to participation in PA ($p = 1.000$). **Conclusion:** Taking into account the observations

from evidence-based reviews in Chapter 1 and the results from Chapter 2, the proposed framework should include an exercise intervention that considers a moderate frequency of three to five times/week, a medium and building up to a higher intensity of 40-80% HRR, shorter sessions of 25-40 minutes per session but building up to 60 minutes where possible, and inclusion of aerobic and resistance exercises with a focus on walking as well as lower body activities. Group sessions should be considered to allow space for social interactions through physical activity which may help work around the barrier of motivation. Patient education on OSA and its consequences, the role of sleep, sleep hygiene, and disease management should also be included as part of the exercise intervention. Importantly, our results provide a basis for further development on this framework to establish an exercise Intervention as an adjunct therapy for OSA patients, specifically in lower income settings. Future studies can explore the efficacy of these exercise interventions in the management of OSA in adults from low income settings.

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CHAPTER 1

LITERATURE REVIEW

1. BACKGROUND

Individuals suffering from obstructive sleep apnoea (OSA) are commonly overweight or obese, and thought to have concurrent underlying chronic inflammation (Alves *et al.*, 2011). Both factors can exacerbate OSA itself and increase the risk for co-morbidities, specifically cardiometabolic disease (CMD) (Calvin *et al.*, 2009). Treatment of OSA with continuous positive airway pressure (CPAP) therapy, the primary gold-standard treatment modality, is effective for moderate and severe OSA (Antic *et al.*, 2011), but remains extremely expensive. It is thus often inaccessible to those in a low-income, under-resourced setting, or without access to healthcare, as is the case for the majority of South Africans. Adherence to CPAP therapy has also been shown to be poor (Marin *et al.*, 2005). It is therefore necessary to explore adjunct therapies for OSA. Since addressing weight loss is a key component of OSA treatment, physical activity in general, and exercise more specifically, may provide the benefits of addressing both weight loss and reducing underlying inflammation in OSA patients, as well as lowering the risk of cardiovascular disease (CVD), depression, and comorbidities that arise from obesity (Carneiro-Barrera *et al.*, 2019). We propose incorporating an exercise regime into the treatment plan for OSA patients, especially in those from under-resourced settings where access to CPAP therapy may be difficult. The aim of this literature review is to investigate the benefits of physical activity (PA) for individuals with OSA, as an alternative treatment plan.

2. OBSTRUCTIVE SLEEP APNOEA

2.1 Aetiology, epidemiology and pathophysiology

OSA is described as a breathing-related sleep disorder wherein ventilation is impaired during sleep, due to the narrowing and collapse of the upper airway (Salman *et al.*, 2020). It is distinct to central sleep apnoea, in which impaired ventilation during sleep results from abhorrent brain control of the ventilatory muscles (Eckert *et al.*, 2007). Further discussion of central sleep apnoea is beyond the scope of this thesis. Deegan and McNicholas (1995) explain that there is a muscle activation imbalance between the oropharyngeal dilator and abductor muscles. The unbalanced force that is produced by these muscles is exceeded by the negative

airway pressure generated by the inspiratory activity of the diaphragm and intercostal muscles resulting in collapse of the airway. This subsequent collapse causes airway obstruction which is alternatively explained as either the suction pressure that is too high or the airway dilating muscles being too weak. OSA is characterized by these recurring episodes of upper airway obstruction during sleep, leading to reduced (hypopnea) or absent (apnoea) airflow throughout the night, and is hence associated with hypoxia (Deegan & McNicholas, 1995).

When oxygen saturation reaches critically low levels, a reflex response is initiated by the sympathetic nervous system causing the individual to gasp to reinitiate breathing and subsequent reoxygenation. While the individual is not always aware of this arousal response, and it does not always lead to a complete awakening, there is an abrupt shift from deeper to lighter sleep. These brief arousals lead to sleep fragmentation, which typically increases time spent in the lighter stages of sleep (i.e. non-rapid eye movement (NREM) stage 1) and diminishes time spent in slow-wave sleep (i.e. NREM stage 3) and REM sleep (Deegan & McNicholas, 1995). These arousals, as well as the rapid reoxygenation of transiently ischemic tissue, lead to the release of reactive oxygen species which activate inflammatory mechanisms followed by a build-up of oxidative stress (Lavie & Polotsky, 2009). Furthermore, repeated episodes of fragmented sleep and hypoxia are thought to reduce heart rate variability during sleep, a marker of autonomic nervous system imbalance, and a predictor of cardiovascular events (Schuster *et al.*, 2016). Untreated OSA has been shown to be associated with an increased number of severe cardiovascular and cerebrovascular events; including myocardial infarction, heart failure, stroke, and sudden cardiac death (Berger *et al.*, 2019).

The main risk factors for the development of OSA include being male, older age (>50 years), obesity, large neck circumference, as well as jaw or upper airway structures that are prone to upper airway collapse (Strausz *et al.*, 2018). Deegan and McNicholas (1995) explain the proposed mechanism for these risk factors as males having an increased pharyngeal and supraglottic resistance compared to females, as well as differences in the distribution of adipose tissue in men, as males tend to have predominantly central fat deposition patterns around the neck, trunk, and abdominal viscera compared to women (Schwartz *et al.*, 2008). Older age is associated with an increase in pharyngeal resistance along with changes in the pharyngeal airway length, size of the parapharyngeal fat pads, and an impairment in the genioglossus negative pressure reflex leading to a reduction in airflow (Eikermann *et al.*, 2007).

The association between a larger neck circumference and higher OSA risk is related to increased fat deposits reported in the pharyngeal walls of obese individuals, leading to increased external compression on the upper airway due to these superficially located fat masses, aiding the collapse of the upper airways. This is especially noted when sleeping in a supine position, as it increases pharyngeal collapsibility by a mechanical effect on pharyngeal soft tissue and lung volume. In addition, with obesity, there are altered interactions of adipokines and adipocyte-binding proteins which affect airway neuromuscular control. As fat accumulates in adipose stores, the signaling pathways encode differences which may produce alterations in the mechanical and neural control of upper airway function during sleep, leading to collapsibility (Schwartz *et al.*, 2008). Anatomical structures such as polyps may contribute to nasal obstruction within the upper airway structures, increasing the resistance of the nasal cavity, hereby leading to an increased effort needed to obtain normal airflow (Deegan & McNicholas 1995).

2.2 Classification

Clinical diagnosis for OSA requires level I or II overnight polysomnography (PSG), which can be completed in a lab or at home. PSG includes measures of respiratory parameters such as abdominal and thoracic breathing effort, nasal airflow, oxygen saturation, and heart rate. Strict criteria based on sleep scoring guidelines published by the American Academy of Sleep Medicine are used to score the PSG for diagnosis (Berry *et al.*, 2012). The resultant Apnoea / Hypopnea Index (AHI) is used to determine the severity of OSA and reflects the number of both apnoeic and/or hypopnoeic events occurring per hour of sleep. Mild OSA is defined as an AHI score of 5-14, moderate OSA as scores of 15-29, and severe OSA as scores ≥ 30 (Littner, 2007).

2.3 Consequences of OSA

Due to pathophysiological factors, resulting from the effects of OSA (figure 1), adverse cardiovascular implications including hypertension, ischemic heart disease, stroke, and arrhythmia may occur.

Proposed mechanisms include neurohormonal dysregulation occurring with apnoea, whereby the peripheral chemoreceptor reflex is activated resulting in a marked sympathetic activation (Angell-James & de Burgh Daly, 1975), endothelial dysfunction due to the intermittent hypoxia impairing the endothelium-dependent vasodilation resulting in atherosclerosis (Feng *et al.*, 2011), and inflammation due to mitochondrial stress resulting in the activation of nuclear factor κ B (Feng *et al.*, 2011).

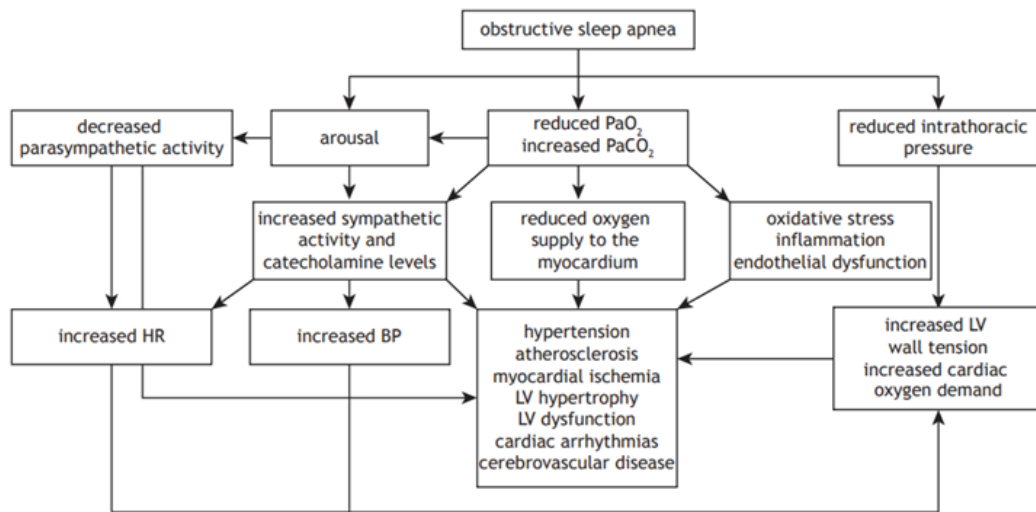


Figure 1. Pathophysiology of the effects of obstructive sleep apnoea on the cardiovascular system. Figure used with permission of de Andrade & Pedrosa (2016).

Metabolic disorders including type 2 diabetes mellitus (T2DM), lipid profile derangements, and non-alcoholic fatty liver disease may also stem from OSA (Strausz *et al.*, 2018). A clinical study by Andrade and Pedrosa (2016) evaluated 100 patients with OSA, with a mean age of 50 years (range 19–75 years). Within this cohort, the prevalence of co-morbidities included hypertension (39%), obesity (34%), depression (19%), gastroesophageal reflux disease (18%), T2DM (15%), hypercholesterolemia (10%) and asthma (4%), with only 33% having no apparent co-morbidities. Furthermore, the presence of co-morbidities appears to be associated with OSA severity since 56% of patients diagnosed with mild OSA, 68% of those with moderate OSA, and 70% of those with severe OSA presented with co-morbidities. In addition, there is a high prevalence of metabolic syndrome in individuals with OSA (Coughlin *et al.*, 2004).

Obesity, specifically, has been positively associated with a higher AHI (Andrade & Pedrosa, 2016). This is thought to be due to individuals with OSA having elevated levels of inflammatory cytokines, such as tumour necrosis factor- α and interleukin (IL)-6, which not only have inhibitory effects on insulin sensitivity in the liver and peripheral tissues (Calvin *et al.*, 2009), but have also been associated with daytime sleepiness (Vgontzas *et al.*, 2008). Thus, visceral obesity may be a pathogenic factor for OSA, both directly and indirectly, through inflammation. Due to these inflammatory mechanisms, there is considerable overlap and interlinked associations between cardiometabolic comorbidities such as T2DM, hypertension, CVD's and obesity, with

OSA. These comorbidities all add additional burden to the health of the individual as well as the healthcare system.

While cardiometabolic comorbidities are of great concern, the many breathing-related arousals experienced throughout sleep in untreated OSA patients result in disturbed, non-restorative sleep. This in turn leads to excessive daytime sleepiness (EDS) (Deegan & McNicholas, 1995), a hallmark feature of OSA, which subsequently impacts other activities of daily living and mood. Specifically, EDS may impair effectiveness and productivity in the workplace and increase the risk of fatigue-related accidents (Meuleners *et al.*, 2015). Thus, in addition to the physical toll OSA can take on an individual, there is also an economic cost due to high levels of presenteeism, productivity losses, legal and insurance costs regarding vehicle and workplace accidents, early retirement, and reduced employment prospects, associated with untreated or poorly managed OSA (Hillman *et al.*, 2006; Sanna, 2013). A meta-analysis by Legar *et al.* (2012) summarizing the economic impact of sleep apnoea found that OSA was associated with reduced cognitive function and had a negative impact on work efficiency and health-related quality of life. In addition, blue-collar workers with severe OSA and EDS were found to have lower work productivity in terms of time management and mental processing/personnel interactions when compared to their counterparts who had mild OSA and EDS (Mulgrew *et al.*, 2007). It is thought that this results from difficulties with memory, concentration, learning of new tasks, performing monotonous tasks, responsiveness, vigilance, and the ability to perform manual tasks in individuals with EDS (Accatoli *et al.*, 2008). Furthermore, poorer work performance translated to a higher prevalence of a change in job duties and job schedules, lower job pay, and missed promotions (Omachi *et al.*, 2009).

In addition to effects on job performance, sleep-related impaired cognition also increases the risk of driving and workplace accidents in individuals with OSA. Mazza *et al.* (2006) showed that OSA patients exhibited longer reaction times leading to poorer driving ability compared to a control group, and Garbarino *et al.* (2015) emphasized this by estimating that 7% of road traffic injuries for a population of male drivers involved in motor vehicle accidents are attributable to OSA and that drivers with OSA have a twofold to eightfold increased risk of motor vehicle crash (Meuleners *et al.*, 2015). This finding is supported by data from a meta-analysis by Sassani *et al.* (2004) who reported that in the year 2000, 800 000 drivers in the USA were involved in OSA-related motor vehicle collisions. These collisions cost \$15.9 billion with 1400 fatalities recorded. The frequency of motor vehicle accidents in patients referred for OSA was also investigated by Fanfulla *et al.* (2021), whereby OSA patients reported on sleepiness at the wheel or sleepiness related near-miss car accidents; self-reported sleepiness at the wheel was reported in 41.3% of patients, and the occurrence of

near-miss car accidents was significantly associated to ESS and oxygen desaturation index (ODI). Untreated or poorly managed OSA has also been shown to have poor mental health consequences. Patients with OSA frequently report fatigue, poor motivation and feeling tired. These symptoms can lead the individual to becoming irritable in their day-to-day activities, affect their work performance, and undermine their relationship with friends/family (Akashiba *et al.*, 2002). The high presence of chronic disease, non-communicable disease in particular, excessive daytime sleepiness, productivity losses, and workplace accidents ultimately increase the socioeconomic cost of a country.

2.4 Common OSA treatment modalities

While CPAP therapy, discussed below, is considered the gold standard treatment for moderate and severe OSA, many other treatment modalities have been investigated as standalone or adjunct therapies owing to the multifactorial nature of OSA. These include surgical treatments, mandibular advancements/adjustments, orthodontic devices, and PA to mention a few. With CPAP therapy, pressurized room air is delivered via an external device attached to the patient via a mask, to help maintain patency of the upper airways during sleep. While the nightly usage of CPAP therapy has been shown to reduce the AHI and excessive sympathetic nervous system activity during sleep, reduce daytime sleepiness and ultimately overall cardiovascular risk, adherence thought to be linked to the comfort of the nasal interface is a major factor in long-term treatment (Marin *et al.*, 2005). Furthermore, obtaining a CPAP device in low-income settings, such as South Africa, where patients are heavily reliant on the public healthcare system, is often challenging due to the lack of equipment availability and the associated cost of the device. Ouédraogo *et al.* (2020), in a prospective study, investigated treatment options for 77 patients from Burkina Faso who presented with suggestive symptoms of OSA. While CPAP therapy was recommended for 41 patients, only nine were able to purchase the device due to cost constraints. In South Africa, the average cost of a CPAP device is about R5 000 or more, with the addition of the mask being a further R1 500 – R2 500 (Raine, 2020). Furthermore, since a reliable power supply is also required for the device to work, CPAP therapy in this setting is not always a viable option.

OSA may be the result of a narrowing at various areas of the upper airway including the soft palate, lateral pharyngeal walls, and the tongue base. If surgical intervention is considered part of the management plan, a combination of surgical procedures is most commonly used. The overall aim is to address multilevel airway abnormalities and improve airway patency in order to normalize sleep quality, improve AHI and oxygen saturation levels, and reduce possible snoring complaints from a bed partner. Due to half to two-thirds of the

nasal cavity contributing to total airway resistance and breathing being primarily nasal during sleep, nasal obstruction contributes to OSA as the increase in negative pressure in the pharyngeal airway leads to pharyngeal collapse (Park *et al.*, 2014). Commonly used nasal cavity surgeries include septoplasty (correction of a deviated septum), polypectomy (removal of abnormal tissue growth which obstructs the nasal cavity), and ablation/reduction of turbinates (Carvalho *et al.*, 2012). Marked improvements were seen in daytime sleepiness, AHI, and respiratory distress index of OSA patients who had undergone a septoplasty and turbinoplasty in a study by Park *et al.* (2014). Nasopharyngeal and oropharyngeal procedures aim to decrease the tissue redundancy and stiffening of the flaccid tissue, while tongue base reduction is targeted to those OSA individuals with a larger base of the tongue due to additional fat deposits (Carvalho *et al.*, 2012). Individuals who have OSA have varying levels of obstruction as well as differing levels of patient characteristics, therefore, translating into variable clinical efficacy. Even with surgical intervention, the use of CPAP is often advised both preoperatively and postoperatively.

Given the cost of CPAP and surgical interventions, and the associated role of obesity in OSA, adjunct therapies to address weight loss and improve systemic inflammation may be of great significance, particularly for overweight/obese patients living in a low-income setting. These adjunct therapies would include dietary and exercise support, either alone or in combination with one another. Given that a recent systematic review and meta-analysis reported low levels of objectively measured PA in OSA patients (Mendelson *et al.*, 2018) and that adults with low levels of PA are more likely to have low-grade inflammation (Wärnberg *et al.*, 2010), the role for exercise warrants attention.

3. PHYSICAL ACTIVITY

PA is defined by Caspersen *et al.* (1985) as “any bodily movement produced by skeletal muscles that results in energy expenditure”. PA is linked to physiological improvements at cellular, metabolic, and systemic levels. Increases in cardiorespiratory fitness and muscle strength are typically experienced following regular participation in PA. These benefits have been associated with a reduced risk for CVD and all-cause mortality, as well as an increase in overall quality of life, brain health, cognition, memory, sleep, and not to mention reduced anxiety levels (McKinney *et al.*, 2016).

There are three main types of physical activity: aerobic, muscle strengthening, and bone strengthening. Aerobic activities are those that make your heart beat faster and in turn your lungs can strengthen due to the increase in breathing that may occur when pushing the body. Aerobic physical activity can also include

all forms of movement, that which is done in your leisure time as well as transport to and from places and can also be of very light intensity such as housework or pushing a grocery cart around the mall, to vigorous intensity such as dancing and soccer. Muscle and bone strengthening can be achieved in your traditional gym setting, but also in unconventional ways such as digging in the garden and climbing stairs. Balance activities and flexibility are also important components of physical activity, to ensure that you are working at your optimal range when it comes to movement.

PA can be subjectively measured by self-report questionnaires, self-report activity diaries/logs and direct observation, or objectively measured by activity tracking devices such as accelerometers, pedometers, heart rate monitors, and armbands. Subjective measurements of PA rely on the participants recall ability to quantify or describe the mode, duration, and frequency of PA. This way of data collection is cost effective and easy to administer, along with allowing for the collection of more descriptive data linked to the participants PA habits. By making use of a PA diary, for instance, it allows for less susceptibility to recall errors, social desirability bias, and measurement bias. Objective measurements provide numerical data on the movement of the body in real time. When considering which PA measure to use, it is important to look at the quality of PA being measured (activity type, intensity, frequency, duration), objectivity of the data and subject burden, cost/burden to administer, and specific limitations of each measurement tool. (Sylvia *et al.*, 2014).

Encouraging the addition of physical activity into everyday life can be done through the use of an intervention framework. The Medical Research Council (MRC) has developed a framework for complex interventions, which allows an exploration of in depth elements of research methods for developing, testing, evaluating, and implementation, with the aim of improving the well-being of those with health/social care needs (Richards & Hallberg, 2015), through a non-linear step process that allows for feedback loops to previous and subsequent stages of the intervention. Understanding how each intervention stage interacts with the next is important to gain an understanding of how the environment can play a role in the intervention design; this allows researchers to address any uncertainties in their intervention and design, as well as their procedural strategies before working toward embedding it into their routine health care (Richards & Hallberg, 2015). Core elements of the framework include considering the context, developing , refining and retesting programme theory, engaging stakeholders, identifying key uncertainties, refining interventions, and the economic considerations of implementation.

3.1 Physical activity as a treatment modality for OSA

By implementing strategies to increase physical activity in the day to day life of individuals, it can be used as a treatment modality for individuals with OSA. Physical activity can be used to reduce the levels of obesity, to increase the levels of fitness parameters such as cardiovascular fitness, and to increase the efficiency of sleep within these individuals.

3.1.1 Benefits of PA for individuals with obesity

A systematic review by Pojednic *et al.* (2022) looked at studies which address the benefits of PA on a holistic spectrum in obese individuals. The PA interventions included sport, high-intensity interval training, aerobic and resistance training, treadmill walking, sprint cycling, and moderate continuous cycling. Findings indicated that participation in sports games was associated with an increase in peak/maximum oxygen uptake ($\dot{V}O_2$), leg strength, and high-density lipoprotein (HDL)-cholesterol (Biddle *et al.*, 2011). Resistance training increased muscle strength (Lubans *et al.*, 2012), and combined aerobic and resistance training had additional improvements such as increases in fat-free mass, $\dot{V}O_{2max}$, and telomere length as was found by Brandao *et al.*, (2020) in a prospective interventional study. Donnelly *et al.* (2009) also emphasized that resistance training can increase fat-free mass and increase the loss of fat mass, which is associated with a reduction in health risks. Treadmill walking and cycle ergometer training resulted in an increase in fat oxidation as noted in a RCT by Colpitts *et al.* (2021), as well as improvements in pulse wave velocity, systolic blood pressure, triglycerides, and lipid hydroperoxides also noted (McNeilly *et al.*, 2012). High-intensity training also showed an improvement in pulse wave velocity, HbA1c, systolic blood pressure and waist circumference (Way *et al.*, 2020), along with an improvement in brachial artery flow-mediated dilation (Sawyer *et al.*, 2016). Brachial artery flow-mediated dilation is a significant predictor of major adverse cardiovascular events, therefore an improvement in this variable could in turn decrease the risk of myocardial infarction, stroke, and CVD death (Yeboah *et al.*, 2007). Barrow *et al.* (2019) demonstrated through a systematic review that participation in high-intensity exercise was also shown to increase individuals' quality of life. Contrastingly, Tai Chi, a low intensity activity, was also found to show an improvement in physical functioning, and Liu *et al.* (2019) highlighted its positive role in physical health and emotional health.

In a systematic review by Barrow *et al.* (2019) on weight management in obese adults at risk for osteoarthritis, studies typically included an exercise frequency of three times per week of durations ranging between 20 – 90 minutes, with aerobic exercise at intensities ranging from 40 - 90% of maximum heart rate (HRmax). Within the South African context, an exercise intervention study by Woudberg *et al.* (2018) analysed the effect of combined aerobic and resistance training in obese female individuals from a low socioeconomic urban area. It was shown that 12 weeks of combined training at a moderate-vigorous intensity for 40 - 60 minutes for four days per week resulted in decreased serum expression of platelet-activating factor acetylhydrolase, an enzyme which is directly correlated to total cholesterol (Kosaka *et al.*, 2001). Altered skeletal muscle lipid profiles were also observed, with decreases in high-density lipoprotein (LDL)-cholesterol over time, associated with reduction in the risk of cardiovascular events. Exercises utilized throughout this 12-week intervention included the use of body weight, resistance bands, and free weights. Squats, lunges, bicep curls, push-ups, and shoulder presses were prescribed at 60 - 70% peak heart rate (HR). This exercise intervention was further analysed by Fortuin-de Smidt *et al.* (2020) to exhibit an increase in insulin sensitivity and peak oxygen consumption, and decreased body weight, BMI and hip/waist ratios. This research was furthered by Mendham *et al.* (2021) to show the exercise intervention resulting in an increase in mitochondrial respiration and content. Ultimately, this exercise intervention was shown to reduce cardiovascular risk factors, as well as improve depressive symptoms, therefore, providing a holistic treatment approach for obese women in a low-income setting (Mendham *et al.*, 2021).

Regular moderate-intensity aerobic exercise has also been shown to improve insulin sensitivity and glycaemic control by facilitating improved glucose regulation (Kirwan *et al.*, 2017). A 0.66% HbA1c decrease was demonstrated by McNeilly *et al.* (2012) in 11 obese individuals diagnosed with impaired glucose tolerance, in which a 12-week exercise intervention of brisk walking at 65% HRmax for 30 minutes per day for five days a week, improved pulse wave velocity, systolic blood pressure, triglycerides, anthropometric measures including body mass, BMI, body fat %, and waist and hip circumference. Lipid hydroperoxides, which are indicative of oxidative stress, also decreased. High levels of oxidative stress have been recognized as an underlying mechanism in the progression from insulin resistance to T2DM as the functioning of the β -cells can get impaired resulting in an under production of insulin which impairs glucose stimulated insulin secretion and fasting hyperglycemia (Tangvarasittichai, 2015), therefore improvements in this variable are beneficial for long-term health benefits. Mean glucose levels, % HbA1c, and insulin concentration, however, remained unchanged in this exercise intervention. Liu *et al.* (2019) found that participation in high intensity

interval training improved body composition (-0.85), HbA1c (-0.29), fasting insulin (-0.46), and cardiorespiratory fitness (4.75mL/kg/min) in patients with T2DM.

Exercise training can lead to a reduction in visceral fat, thereby reducing the pro-inflammatory cytokines (Wärnberg et al., 2010). It has been suggested that this will in turn enhance control of the upper airway musculature thereby avoiding collapse during sleep (Mitchell *et al.*, 2014). Although exercise can increase inflammatory cytokines, such as IL-6, which when elevated for sustained periods of time can be predictive of obesity and type II diabetes (Qu *et al.*, 2014), the transient fluctuations noted during PA appear to have a positive protective effect. The risk of insulin resistance induced by tumour necrosis factor-alpha and interleukin-1 beta can be reduced, seeing as IL-6 inhibits these pro-inflammatory cytokines (Pedersen, 2007). The increase in these cytokines is dependent on exercise intensity and duration, as well as the amount of muscular mass involved in the activity (Shaw *et al.*, 2018) therefore a protocol that is evidence-based is necessary to avoid the risk of sustained elevations.

3.1.2 Benefits of PA on cardiorespiratory fitness and cardiovascular parameters of individuals with OSA

Cardiorespiratory fitness, the ability of the circulatory and respiratory system to supply oxygen to muscles during PA, is known to have unique health and longevity benefits. An enhanced cardiorespiratory fitness can lower the risk of CVDs, major adverse cardiac events, and overall mortality (McKinney *et al.*, 2016). A meta-analysis of three random control trials (RCT's) investigating the effects of exercise training in OSA patients on AHI, BMI, sleep efficiency, Epworth Sleepiness Scale score and $\dot{V}O_2$ peak found an 18% average increase in the $\dot{V}O_2$ peak following exercise training, a marker of cardiorespiratory fitness (Iftikhar *et al.*, 2014).

The effect of exercise training on patients with chronic heart failure and sleep apnoea is one that is commonly studied; this is due to the impact of the repeated elevations in systemic BP and increased sympathetic nervous system activity which arise from each apnoea. The combination of decreased stroke volume, suppression of sympathetic inhibitory effects, increased left ventricular (LV) afterload and faster heart rate disposes the individual to cardiac ischemia, LV hypertrophy, LV enlargement, and ultimately heart failure (Khattak *et al.*, 2018). Servantes *et al.* (2012) compared two groups of participants with chronic heart failure and OSA who underwent a three-month intervention consisting of aerobic training (group A), and aerobic

training + resistance training (group B), to a control group. Participants in group A and group B were asked to complete three sessions per week in the first and second month, and progress this to four sessions per week in the third month. Activities were performed on non-consecutive days. As with many other studies, the aerobic training component focused on walking as a mode of activity. Participants were required to walk in the street/a park for 30-45 minutes along with a warm-up and cool down. The aerobic + resistance group (group B), added some resistance exercises to the intervention i.e. three exercises for the upper body, and four exercises for the lower body. The intensity was kept at 30-40% of the maximum weight that an individual can lift for a given exercise for one-repetition (1RM), at 12 repetitions x 1 set, with a 1-minute rest period between exercises. This range increased to 16 repetitions in the third month of the intervention. Individuals were presented with a manual that contained illustrations of the strengthening and stretching exercises, allowing for a safe, progressive, self-monitored exercise programme with guidelines on how to navigate through frequency and targeted heart rate values. Both groups A and B experienced a marked decrease in minute ventilation/volume of carbon dioxide produced (VE/VCO_2) during exercise, whereas the untrained group (group C) experienced no change. This is clinically significant as an abnormally high VE/VCO_2 is associated with a higher risk of cardiovascular events (Ingle, 2008). As expected, group B also reported a greater increase in muscle strength and endurance compared to group A and the control, due to the addition of resistance training.

Dobrosielski *et al.* (2015) performed a study following American College of Sports Medicine (ACSM) guidelines that combined moderate and vigorous intensity exercise performed on either a treadmill, cycle ergometer, or stair stepper with the aim of achieving a total energy expenditure of >500-1000 metabolic equivalent of tasks/min/week for each participant who was obese with OSA. Participants accumulated 45 minutes of total cardiorespiratory conditioning per session at incrementally increasing intensities from 60 to 85% HRmax. They also did two sets of 10-15 reps of the following exercises: leg extensions, latissimus dorsi pull downs, leg curls, bench press, leg press, shoulder press and seated mid rowing. The exercise programme was coupled with a dietary intervention. Over the course of three months, reductions in body weight (9%), total body fat (5%), trunk fat (8%), and waist circumference (6%) were observed, accompanied by improvements in aerobic capacity (20%).

3.1.3 Benefits of PA on sleep parameters of individuals with OSA

Carneiro-Barrera *et al.* (2019) systematically reviewed 13 RCTs and 22 uncontrolled before-and-after studies which reported on lifestyle interventions used in OSA patients to improve AHI, ODI, EDS, and secondary OSA measures. The lifestyle interventions included dietary weight loss, moderate exercise training, sleep hygiene, and combinations thereof. Of the reviewed studies, a reduction in AHI was seen in 94% of the before-and-after studies, and 92% of the RCT's, a reduction in ODI was seen in 100% of the studies, and a reduction in EDS was seen in 94% of the before-and-after studies and 100% of the RCT's. Collectively, the studies revealed significant improvement in AHI, ODI, and EDS following an intervention period.

Evidence from this review suggests that dietary, exercise and sleep interventions all have the potential to improve sleep parameters in OSA patients, with no single intervention type being better than another. It may be inferred that an exercise intervention contributed to this overall positive impact, thus, when aiming to improve the sleep parameters and daytime function of OSA patients, there appears to be a role for exercise, especially when used alongside dietary and sleep interventions. One thing to consider in resource-constrained settings, however, might be limited access to healthy foods or exercise facilities.

A 2014 meta-analysis (Iftikhar *et al.*, 2014) examining the impact of pure exercise training in three OSA cohort studies showed an average reduction in AHI of 32% (6.27 events/hour) from baseline. This was accompanied by an average improvement in sleep efficiency of 8%, as well as a 28% average reduction in daytime sleepiness across all included studies. Kline *et al.* (2011) investigated the effects of exercise training on OSA severity symptoms and sleep quality in 43 sedentary overweight and obese adults with OSA. Participants underwent 12-weeks of moderate-intensity aerobic activity (four treadmill sessions per week, 60% of heart rate reserve, totaling 150 minutes per week) combined with resistance training twice per week. The supervised resistance training programme comprised two sets (10-12 reps) of eight exercises (shoulder press, latissimus dorsi pull down, leg extension/flexion, chest press, upright row, leg press, biceps curl/triceps extension and abdominal crunches). Although the participants did not show a decrease in body weight, both AHI and ODI reduced, and the time spent in N3 sleep increased.

In a similar study, Redolfi *et al.* (2015) noted a small increase in the time spent in N3 sleep in individuals diagnosed with mild to moderate OSA, following one week of two periods a day of 45 minutes of moderate-speed walking. An increase in time spent in N3 sleep was also noted after OSA participants underwent a four-month exercise programme consisting of three 60-minute sessions per week in which participants did

stretching and cycle ergometry at 10% below their respiratory compensation point (McSharry *et al.*, 2013). Following an intervention based on ACSM guidelines, Dobrosielski *et al.* (2015) noted an increase in sleep time by 27 minutes, and an average reduction of ten AHI events per hour of following the regime. Similar findings were documented in OSA patients with heart failure whereby time spent in N3 sleep increased, AHI improved by 36%, and minimal oxygen saturation during sleep also improved by 5% following a four-month exercise programme. This programme comprised three 60-minute supervised sessions each week that included stretching, 25 minutes of cycle ergometry aerobic training, and ten minutes of strength exercises (Ueno *et al.*, 2009). The improvement in N3 sleep duration is particularly important for OSA patients. Untreated or poorly managed OSA results in disturbed, unrefreshing sleep, often characterized by reduced N3 and increased N1 sleep. Using resistance training combined with aerobic training, Servantes *et al.* (2012) marked a decrease in AHI, with group A (aerobic training only) experiencing reductions in hypopnea events and group B (aerobic combined with resistance) reductions in hypopnea and apnoea events. These data suggest that the inclusion of resistance training into an exercise intervention allows for a reduction in the number of more severe periods of airway obstruction. Collectively, these studies demonstrate the potential benefit of exercise training for OSA patients beyond simply facilitating weight loss.

Finally, Bughin *et al.* (2020) reported that an eight-week exercise intervention in OSA patients which included both upper and lower body resistance training at 60% of 1RM, combined with educational sessions around OSA, and PA, reduced AHI during REM sleep specifically. This is important since having more OSA episodes during REM sleep has been associated with an increased risk for hypertension, non-dipping of nocturnal blood pressure, increased insulin resistance, and impaired human spatial navigational memory (Alzoubaidi & Mokhlesi, 2016). The prevalence of non-dipping in blood pressure has been associated with left ventricular hypertrophy, angina, myocardial infarction, ischemic stroke, as well as a worse cardiovascular prognosis with increased target organ damage and even death (Chobanian *et al.*, 2003). Thus, an improvement in AHI during REM sleep may be critical to reducing the risk for metabolic and cardiovascular co-morbidities associated with OSA.

It is important to note that sleep hygiene is a factor to consider when assessing the impact that physical activity can have on sleep. Ackel-D'Elia *et al.* (2012) investigated the effect of exercise combined with sleep hygiene in individuals with OSA who were already undergoing CPAP treatment. Participants underwent two months of an exercise training intervention, which consisted of three sessions per week. In the second month, they also incorporated sleep hygiene adjustments, whereby they were instructed to avoid alcohol, sedative

medications, and heavy meals before going to sleep to maintain regular sleep times and to avoid sleeping in a supine body position. This was followed by a one-week washout/no treatment period. Participants in the intervention group demonstrated fewer awakenings per night and reported “feeling better when they awoke” compared to the control group (no intervention). Noteworthy is that the decrease in subjective sleepiness was maintained after the washout period for those within the intervention group.

3.2 Additional benefits of PA and alternate exercises in the management of OSA, with special reference to the effects on the airway

There is a further role that PA can play in improving the symptoms of OSA. Andrade *et al.* (2016) showed that long-term regular exercise can increase upper airway muscle activation, which in turn increases the upper airway diameter and reduces airway resistance. Endurance exercise has also been shown to reduce low-grade inflammation, which in turn should improve upper airway muscle tone and reduce resistance. This may reflect a co-activation effect, whereby skeletal muscle activation through exercise transfers to co-activation of upper airway muscles. When assessing co-muscular activation throughout the body, Haxhiu *et al.* (1984) and Hussain *et al.* (1991) found that electrical stimulation of the gastrocnemius muscle nerve in dogs resulted in an increase in the tone and peak EMG activity of the genioglossus muscle. This may suggest that activation of the lower limbs can result in a co-activation of the upper airway dilator muscles, but has not been replicated in humans. Pharyngeal collapse during sleep can therefore be opposed in patients with OSA who participate in regular exercise (Peng *et al.*, 2022).

Sengul *et al.* (2011) assessed the effect of a 12-week breathing and PA intervention on pulmonary function, AHI, and quality of life in persons with OSA. Participants completed 15-30 minutes of breathing exercises, and 45-60 minutes of aerobic exercises three days per week. The breathing exercises included pursed lip breathing, diaphragmatic breathing, thoracic expansion exercises, and postural exercises. The aerobic exercise component was performed at submaximal intensities (60-70% $\dot{V}O_2\text{max}$) and consisted of slow jogging, calisthenics and stretching. Improvements were seen in aerobic exercise capacity (measured via forced vital capacity and forced expiratory volume in the first second as a percent of the predicted forced vital capacity), $\dot{V}O_2\text{max}$ upon follow up exercise testing, and improvements in the degree of leg tiredness after exercise, perceived severity of dyspnoea after exercise, AHI, as well as functional outcomes assessed by questionnaires (sleep quality and health related quality of health).

One of the factors that contributes to OSA is the accumulation of fluid in the legs that shifts to the neck during sleep due to gravitational forces. This fluid accumulation in the legs is increased in individuals who have a sedentary lifestyle and PA counteracts this by activating musculo-venous pumps that assist with circulation (Winkel & Jørgensen, 1986). Redolfi *et al.* (2015) introduced OSA patients to PA by asking them to walk twice a day at a moderate speed for 45 minutes, for just one week. They observed a 40% reduction in overnight fluid shift, a 64% reduction in nocturnal neck enlargement, and a 30% reduction in AHI for these patients. Hence it is evident that PA can attenuate the severity of OSA without a weight loss mechanism, but by means of activation of the musculo-venous pumps to counteract the overnight collection of fluid around the pharynx from the legs. White *et al.* (2015) also targeted these nocturnal fluid shifts in OSA patients by using below-the-knee compression stockings during the daytime, whereby a significant decrease in AHI was also noted. Therefore, patient education surrounding the use and availability of compression stockings within clinics around South Africa, as well as a push to include PA in your day-to-day activities may be an additional tool when addressing management of OSA in a holistic manner.

Apart from the traditional aerobic, resistance and respiratory training, Guimarães *et al.* (2009) looked at the addition of oropharyngeal exercises as part of an intervention for OSA patients. The goal of these exercises was to target tongue repositioning and promote mandibular elevation. Individuals were required to perform isometric and isotonic exercises of the tongue, soft palate, and lateral pharyngeal wall over a period of three months. These included actions such as suction, swallowing, chewing, breathing, and speech. The aim of the muscular exercises was to improve the tone, tension, and mobility of the oropharyngeal muscles and soft tissue with the aim of reducing airway closure during sleep (Diaféria, 2017). When targeting the muscles of the soft palate, tongue, and face, they were asked to (a) pronounce oral vowels intermittently and continuously daily for three minutes, (b) perform various movements around the mouth with the tongue, and (c) mimic facial expressions to recruit the facial musculature. Balloon blowing, phonation of open vowels, and tasked chewing were also included. The group that underwent this alternative treatment of oropharyngeal exercises experienced an 8.7 event/hour reduction in AHI (i.e. 39% decrease in OSA severity), a 2% increase in lowest oxygen saturation during the night, a 3% reduction in neck circumference, snoring, daytime sleepiness, as well as an improvement in quality of sleep scores. This suggests that remodeling of the upper airway through non-surgical means is another way of reducing OSA severity, without a reduction in BMI or weight.

4. Considerations for OSA management in low-income settings

a. Effect of SES on access to healthcare and health status

Socioeconomic status (SES) heavily impacts the risk factors for CVD, and thus increases the overall impact of a disease, such as OSA, on cardiometabolic health. Low SES has shown to be related to poor health, and closely related to increased mortality and morbidity from CVD (Tarasiuk *et al.*, 2006). Tarasiuk *et al.* (2006) evaluated whether SES was a CVD risk factor among OSA patients requiring treatment. They found that of the OSA patients living in a low SES environment in two regions in Israel, 53% of the Arabs, being immigrants (Bedouin and non-Bedouin), had severe OSA, 27% had CVD, and 28% had an Epworth Sleepiness Scale (ESS) score > 10 when compared to the native Jews. They observed that for each decrease in the category in income level category (proxy for SES), the independent risk for CVD in OSA patients increased. The authors hypothesized that this observation relates to behaviours such as smoking, poor diet, excessive alcohol consumption, physical inactivity, and nonattendance to health checkups that are more common in low SES environments as well as limited access to treatment. Not only was the prevalence of OSA higher in low SES populations, but those from low income levels also had a higher % of individuals that have CVD ($p=0.010$), ischemic heart disease ($p=0.048$), and diabetes ($p=0.034$) when compared to those from a high income level (Tarasiuk *et al.*, 2006).

From a South African perspective, Roche *et al.* (2020) found, through a cross sectional study, that in an older cohort of low SES South Africans living in a rural setting, 29% had undiagnosed OSA, 61% were overweight/obese, and 60% were hypertensive. All were untreated for OSA but given their high levels of comorbidities (obesity and hypertension), there is a need for OSA management to include PA to help address obesity and hypertension, as well as OSA severity. Being older, having a higher body mass index, and having a higher waist circumference were also associated with OSA.

Similar trends were observed in a cross-sectional study by Ozoh *et al.* (2014) which assessed for OSA risk and excessive daytime sleepiness in a Nigerian cohort of inpatient and outpatient individuals from the Lagos University Teaching hospital, from a low SES. The risk of OSA was high in 36% of the individuals according to the results of the STOP-BANG questionnaire, and 24% of the population experienced excessive daytime sleepiness. In addition, hypertension was present in 42% and diabetes in 11% of the population, with 8% of those with hypertension having resistant hypertension. As found by Roche *et al.* (2021), none of these

individuals at high risk for OSA had been formally diagnosed or provided with any treatment options. Similarly, Poka-Mayap *et al.* (2020) found in their analysis of patients admitted to a tertiary referral hospital in Cameroon, 57.7% of the patients had OSA, with 31.5% being categorized as moderate-severe OSA (diagnosed with a portable sleep monitoring device), and none of the patients were aware of their diagnosis. On one hand, these findings suggest a lack of awareness or diagnostic availability among clinicians regarding OSA in these three African settings. One might also assume then that management of this apparently under-diagnosed disorder in under-resourced environments may well be a challenge. This emphasizes the need for alternate or added treatment strategies that may improve not only OSA severity but also the associated sequelae and comorbidities. Patient education is, therefore, necessary for both healthcare providers as well as the general population.

When assessing health care, specifically within a South African setting, a large percentage of health care costs have been found to be attributed to managing and treating weight-related diseases. Boachie *et al.*, (2022) found that about 53% of the total annual healthcare cost, which translates to approximately 15% of the government health expenditure, is attributed to the overweight-obesity cost of the country. Per person the annual cost of overweight and obesity is approximately R2,769. Participation in PA can reduce the impact of cardiovascular disease, musculoskeletal disorders, respiratory diseases and digestive system diseases, seeing as an increased BMI is associated with a higher prevalence of these health complications (Wen *et al.*, 2011).

In 2020, it was found that approximately 12 million people receiving treatment within the public health care sector had a weight related disease (Boachie *et al.*, 2022). In South Africa, healthcare is provided at no cost to individuals who are unemployed. This healthcare cover includes the use of intensive care services and chronic medications. These costs per patient, however, still need to be covered by the government as the cost of daily consumables, ward overheads and medication, as well as training of the healthcare workers still need to be carried out. Mahomed & Mahomed (2018) used a mixed methods costing approach to demonstrate that the daily cost per patient in an unspecialised intensive care unit is R22 870. Therefore, not surprisingly, there is also an association between length of stay and cost per patient, with the more critical the patient, the higher the cost to the government/state. In addition, Individuals living with obesity are also more likely to use healthcare services, take more prescribed medication, have more outpatient visits compared to those of a lower weight and potentially have poorer recoveries if admitted to an intensive care unit (Cecchini, 2018).

Furthermore, Individuals from lower SES settings, who are unemployed, may not receive regular health care, leading to the assumption that when admitted to a hospital, the likelihood of longer stay is increased. South Africa has one of the highest income inequality and poverty rates, with high structural unemployment levels as well (Netshitenzhe, 2013). In the first quarter of 2018, youth unemployment stood at 38.2%, therefore there is a large proportion of the country that is unable to contribute to economic growth (STATSA, 2018). Many South Africans come from lower SES environments, as South Africa is considered to have high rates of child food insecurity and malnutrition, with 85% of food insecurity and 7.9% of malnutrition as reported by Alaba *et al.*, (2021), which also poses as a substantial health problem. The World Bank, in 2015, stated that South Africa has both ends of malnutrition, as undernutrition is even prevalent in obese children. The poverty headcount ratio was reported as 55.5% in 2018 (STATSA, 2018), which had risen dramatically from 31% in 1995, and continues to rise as it was recorded at an estimated 63% in 2022 (World Bank, 2015). Weak structural growth, an increasing population and the COVID-19 pandemic have only exacerbated the existing SES challenges, with the rising fuel and food prices contributing to these heightened poverty rates with the poorest in society being affected by deprivation, hunger, and unemployment (Chetty, 2021).

The cost of managing and treating CVD and endocrine disease relating to overweight and obesity mainly stems from hypertension and diabetes. PA interventions have been shown to decrease the prevalence and severity of hypertension and diabetes (Wen *et al.*, 2011), leading to the conclusion that the design of a preventative intervention that can be delivered at a population level with an aim to reduce incident cases and severity of the diseases, with less medications required, will have a positive impact on the health care costs within South Africa and lower the overall NCD healthcare cost in the long term.

The evidence from the reviewed literature suggests that PA along with other lifestyle changes may greatly improve many of the multifactorial pathophysiological pathways involved in the development, severity and sequelae of OSA, along with providing a relief on the healthcare costs of the country. Given the promising evidence base for the role of exercise as an adjunct therapy for OSA patients, we would ultimately like to design an exercise intervention programme for implementation as an adjunct therapy for OSA patients, particularly in under-resourced public healthcare settings such as those found in South Africa.

Hence the aims and objectives for this thesis are:

Aim 1: To understand the nature of current PA habits, perceptions, and barriers of individuals with obstructive sleep apnoea (OSA group) in comparison to a control group of individuals without OSA (CON group).

Objective 1.1: To use a combination of custom and validated questionnaires to describe and identify themes related to current and past PA habits, reasons for possible cessation of exercise, the potential facilitators and barriers to exercise, preferred exercise modalities and settings, and suggestions relating to possible exercise interventions in OSA and CON participants.

Objective 1.2: To use a detailed diary to learn about actual current PA habits (mode of PA/exercise, frequency, intensity, duration) over the course of a week in the OSA and CON participants.

Aim 2: To design, with the use of the MRC framework, an exercise intervention framework for OSA patients, which can be implemented in an under-resourced setting such as the public healthcare system in South Africa.

Objective 2.1: To use information obtained in Aim 1 and the literature to create a risk-stratified exercise intervention framework, comprising both supervised and home-based activities, intended to ameliorate co-morbidity risk and OSA severity in OSA patients.

CHAPTER 2

The design of an exercise intervention framework, to be implemented as a modality of treatment, for individuals with obstructive sleep apnoea, in the South African public healthcare setting.

1. INTRODUCTION

Poor sleep quality attributes have been negatively associated with both short- and long-term health outcomes (Medic *et al.*, 2017). Sleep disorders and resultant poor sleep quality have emerged as being related to cardiometabolic disease (CMD) risk, including obesity, hypertension, type 2 diabetes mellitus (T2DM), and cardiovascular disease (CVD) (Andrade & Pedrosa, 2016; Schwartz *et al.*, 2008; Wärnberg *et al.*, 2010). There is evidence to suggest that disordered sleep may play an important role in health imbalances and may in fact represent a partially modifiable risk factor (along with diet and PA, PA) for CMD risk in general and cardiometabolic health aberrations specifically (Koren *et al.*, 2016). This suggests that good sleep quality is important for optimal cardiometabolic health.

While insomnia represents the most common sleeping disorder, the second most frequent sleeping disorder is obstructive sleep apnoea (OSA) (Partinen & Hublin, 2005). The current gold standard treatment plan for those with obstructive sleep apnoea is nightly usage of continuous positive airway pressure (CPAP) (Kushida *et al.*, 2006). For patients living in low-income settings, such as is common in South Africa, obtaining a CPAP device is often challenging due to the lack of equipment availability and the associated cost of the device (Ouédraogo *et al.*, 2020). Thus, alternative and complementary therapies, to be used by OSA patients until such time as CPAP therapy can be commenced, are needed. Therapies which target weight, for example, might be beneficial, since not only have OSA patients been observed to have higher levels of obesity than individuals without OSA, there is also some evidence to suggest that a higher BMI, which is a marker of obesity, is associated with OSA severity (Schwartz, 2008). Lifestyle interventions focusing on diet and PA may therefore be viable adjunct therapies in this context.

The role of lifestyle interventions in the treatment of OSA severity in older adults has, until relatively recently, received little attention in the literature. Dietary interventions, linked to weight management, are commonly used to address weight management, and among patients with OSA, interventions that include dietary components have been shown to improve OSA severity (Carneiro-Barrera *et al.*, (2019)). The role of a

structured diet management plan on OSA severity symptoms, nocturnal oxygen indices and subjective sleep parameters was investigated by Rokou *et al.*, (2022); a Mediterranean diet was shown to exhibit greater weight reduction than a prudent diet after 6 months, along with reductions in AHI during REM sleep.

Studies that have incorporated dietary interventions along with an exercise intervention have shown a significant reduction in AHI, ODI, and EDS (Carneiro-Barrera *et al.*, 2019), along with significant improvements in cardiometabolic and neurobehavioral outcomes (Barnes *et al.*, 2009). An alternative approach to weight loss is to focus on increasing PA levels alone, without dietary intervention. One study has shown that individuals with mild and severe OSA who exercised for more than four hours per week were able to reduce AHI (Awad *et al.*, 2012). A similar study also observed an improvement in AHI among OSA patients taking part in an exercise intervention, but with no accompanying change in BMI. This suggests that exercise may impact OSA severity via pathways other than weight loss (Sengul *et al.*, 2011). Proposed mechanisms include exercise increasing upper airway muscle tone, limiting the propensity for airway collapse during sleep, and better distribution of body fat such as a reduction in pharyngeal fat accumulation, therefore reducing compression of the upper airway during sleep (Awad *et al.*, 2012). Some studies are now emerging to show that the combined use of CPAP therapy with weight loss is more beneficial for patients compared to CPAP therapy alone (Servantes *et al.*, 2012). Furthermore, the prevalence of metabolic syndrome was reduced by 45% in a study that intervened with one year of CPAP therapy and weight reduction (Oktay *et al.*, 2009), compared to a 20% reduction in a study whose participants did not lose weight (Mota *et al.*, 2011).

Other benefits of increased PA in OSA patients may relate to mental health. A cross-sectional study by Simpson *et al.* (2015) has observed that diagnosed depression was more common in individuals with OSA than those without OSA. Furthermore, those with low levels of PA or sedentary occupation also reported more depression and fatigue, higher blood pressure, higher levels of the inflammatory biomarker C-Reactive Peptide, and more severe OSA symptoms compared to those who were more active (Simpson *et al.*, 2015). Thus, the incorporation of PA into treatment plans for individuals with OSA may represent a holistic approach.

In the South African context, adjunct therapies for OSA would be welcome given the economic restraints experienced by a majority of the population who are reliant on the public healthcare system (Naidoo, 2012). Not only is purchasing a CPAP device preclusive, but simply increasing PA levels is challenging given the limited access to safe outdoor exercise spaces or affordable indoor gyms and clubs with staff suitably

qualified to supervise patients with significant CVD risk and co-morbidities. Given the promising evidence base for the role of PA and exercise as an adjunct therapy for OSA patients, we aim to ultimately design, with the use of the COM-B model for behaviour change which takes into consideration the capability (C), opportunity (O), and motivation (M) of individuals' as three key factors capable of changing behaviour (B), and implement an exercise intervention as an adjunct therapy for OSA patients, particularly in the public healthcare setting in South Africa. The aim of this study is to design a framework, that includes exercise as a feasible intervention, to be used in the treatment of OSA severity, particularly catered to those from an under-resourced setting.

2. METHODS

2.1 Study design

This is a secondary analysis of data already collected as part of a larger study investigating "PA and sedentary behavior among patients with obstructive sleep apnoea in South Africa". Both the parent study and the secondary analysis were approved by the University of Cape Town's Human Research Ethics Committee - (HREC Ref: 142/2021 and 577/2022 respectively). The parent observational study made use of custom and validated questionnaires, including open-ended questions answered by adults diagnosed with moderate to severe OSA and control participants with no OSA. Interested participants were required to visit the Health through Physical Activity, Lifestyle and Sport Research Centre at the University of Cape Town on two separate occasions for approximately two hours in total. During these visits, the researcher explained the study in detail to the participants, and participants who agreed to take part in the study signed an informed consent form and completed detailed questionnaires (Appendix 1). The researcher measured participants' weight, height, waist and neck circumferences, and resting blood pressure. Participants were then asked to complete a PA and sleep diary for one week (Appendix 2). All data were de-identified and entered into a master spreadsheet. For this secondary analysis, we were provided with the specific variables needed to address our study aims described above.

Sample size calculations for the parent study were based on expected differences between the three main outcome variables (i.e. weekly habitual physical activity levels, daily sleep efficiency and resting blood pressure) between OSA patients with and controls without OSA. For a power of 80% and at alpha level of 0.05, 34 participants were required (17 per group) for an expected mean \pm SD difference of 60 \pm 60min exercise per week; 48 (24 per group) for an expected mean \pm SD difference of 5 \pm 6% in sleep efficiency; and 52 (26 per

group) for an expected mean difference of 20 ± 25 mmHg in BP. Therefore, 30 per group were recruited to allow for drop out.

2.2 Participants

The OSA group comprises men and women ($n=18$, >18 to 65y of age) previously diagnosed with moderate to severe OSA ($AHI>15$) using polysomnography. Diagnosis of OSA was confirmed via questionnaires and an AHI scale. The control (CON) group contains adults ($n=19$) matched to the OSA group for age and sex, with no previous diagnosis of OSA and no symptoms or signs of OSA as confirmed on a validated OSA screening tool – the STOP-Bang questionnaire (Chung *et al.*, 2016). Exclusion criteria for all participants were as follows: younger than 18y or older than 65y of age; not ambulatory (i.e., makes use of any walking aid); any recent (two month) change in their usual PA or sleep habits. An additional exclusion criterion for the OSA group only included an AHI of <15 , while those for the CON group only included (i) a previous diagnosis of OSA ($AHI \geq 5$), (ii) a STOP-Bang risk score of >4 or (iii) an affirmative answer to the STOP-Bang question “Has anyone observed you stop breathing during your sleep?”. CON group individuals identified during screening as being at an increased risk of suffering from OSA were referred to their healthcare provider for further assessment and investigations. Participants for both groups were recruited using a media release distributed through various media channels (e.g., newspaper, social media) and word of mouth.

2.3 Procedure and data collection

We describe here the methods of the parent study that are relevant and specific to the analyses of this study.

2.3.1 Questionnaire

The questionnaire (Appendix 1) captured patient demographic, socioeconomic status, and medical history information to both characterize participants, and determine eligibility for the study. OSA severity was determined using the AHI obtained from the diagnostic sleep study for each OSA participant. Socio-economic status was determined using years of education received (from Grade R), and employment status. The STOP-Bang questionnaire, which has a sensitivity of 89.1%, 90.7% and 93.9% to screen for all ($AHI \geq 5$), moderate-to-severe ($AHI \geq 15$) and severe ($AHI \geq 30$) OSA, respectively (Mark *et al.*, 2021), was used to screen participants for OSA risk, accounting for the following eight risk factors: excessively loud snoring, excessive

daytime tiredness, observed apnoeas during sleep, high blood pressure, body mass index (BMI) $>35\text{kg/m}^2$, $>50\text{y}$ of age, neck circumference $>43\text{cm}$ (men) and $>41\text{cm}$ (women), and being male.

Customized questions asked participants to report on current (within the past month) and past PA and exercise habits; these included years, mode, frequency, duration, and intensity (rated on a subjective scale of 1-10; 1 being 'very light, heart rate low, a sensation of "I could do this all day"', and 10 being 'vigorous, heart rate near max, a sensation of "I can't keep this up for too long"'). Intensities of exercise were not categorised with %HR or any specific range measurements. They were also asked to report on their satisfaction with current exercise habits, reasons for not exercising, and barriers to exercise. Lifestyle factors were also recorded; this included smoking status which was categorized as a current regular smoker being an individual who smokes at least one cigarette a day for at least one year, and alcohol consumption status which was categorized as consuming at least one alcoholic beverage per week for at least one year. In addition, the questionnaire incorporated the following validated questionnaires:

2.3.1.1 The Short Form (36) Health Survey (SF36)

This validated and reliable (Brazier *et al.*, 1992) 36-item tool assesses a person's mental and physical health status and perceived quality of life. Questions cover eight domains of health: limitations in physical activities because of health problems, limitations in social activities because of physical or emotional problems, limitations in usual role activities because of physical health problems, bodily pain, general mental health (psychological distress and well-being), limitations in usual role activities because of emotional problems, vitality (energy and fatigue) and general health perceptions (Lins & Carvalho, 2016). *Outcome variables:* scores for each of the eight subscales and a global health score.

2.3.2 PA diary

Participants were asked to complete a PA and sleep diary over a period of seven consecutive days. This enabled assessment of current PA habits: number of days per week engaged in PA and exercise, PA/exercise modes (e.g., walk, gym, tennis), and the number of sessions per week, minutes per day, and total minutes per week engaged in the relevant exercise/PA mode. Evidence obtained from the literature review was used in conjunction with the PA diary when constructing guidelines for the framework.

2.3.3 Clinical measures

2.3.3.1 Anthropometric measurements

Height (m), weight (kg), waist and neck circumferences (cm) of all participants were measured by the same individual. BMI was calculated as weight (kg) / height (m)². Participants were classified as normal weight if BMI was $\leq 25 \text{ kg/m}^2$, overweight if BMI $> 25 \text{ kg/m}^2$ but $< 30 \text{ kg/m}^2$ and obese if BMI $\geq 30 \text{ kg/m}^2$. *Outcome variables*: waist and neck circumference (cm), BMI (kg/m^2), and BMI category.

2.3.3.2 Blood pressure (BP)

Resting BP was measured in participants following ten minutes of seated rest. Readings were taken three times at one-minute intervals using an appropriately sized cuff and a manual BP sphygmomanometer and averaged to obtain final results (Park *et al.*, 2019). *Outcome variables*: resting systolic blood pressure (SBP), and diastolic blood pressure (DBP).

2.3.4 Statistical analysis

Data are presented as mean \pm standard deviation, median [interquartile range], or count (%). The Shapiro-Wilks test was used to determine whether the data were normally distributed. Between-group comparisons were conducted using independent t-tests, Mann-Whitney U, Fisher's Exact, or Chi-Squared tests. In addition, a qualitative quasi-deductive research approach was used to identify common themes related to perceptions, enablers, and barriers to PA, as well as preferred modes of PA/exercise in both groups of participants.

All statistical analyses were performed using IBM SPSS software (version 25.0, IBM, Armonk, NY, USA) with significance accepted at $p \leq 0.05$.

3. RESULTS

3.1 Participants characteristics

Table 1 displays the descriptive and clinical characteristics of the OSA and CON participants included in the study. The OSA group had a higher BMI ($p < 0.001$), larger neck and waist circumferences ($p < 0.001$), and higher SBP ($p = 0.039$) than the CON group. In addition, the presence of self-reported chronic conditions was higher

in the OSA group (n=16) than in the CON group (n=9) ($p = 0.007$), and more of the OSA group suffered from hypertension ($p=0.031$) and diabetes ($p=0.019$).

The proportion of smokers was not different between the OSA and CON groups ($p=0.604$).

The mean number of years of education was reported to be 22 years and 16 years for CON and OSA respectively, with no significant difference between the two groups ($p=0.090$). All individuals of the CON group are employed, with only 83.3% of the OSA group being employed, as 16.7% are retired.

The impact of health limitations on certain activities, as exhibited through the SF-36 questionnaire, was not different in any subscale between the OSA and CON groups.

Table 1. Descriptive and clinical characteristics of the CON and OSA groups.

	CON group (N=19)	OSA group (N=18)	
<i>Descriptive characteristics</i>			
Age	56 [13]	59 [14]	0.879
Males	15 (79)	14 (78)	0.931
Smoker	1 (5.3)	2 (11.1)	0.604
Alcohol consumer	6 (31.6)	6 (33.3)	0.909
Employed (full time/part time)	19 (100)	15 (83.3)	0.105
Retired	0 (0)	3 (16.7)	0.105
Years of education	16 [3]	15 [4]	0.090
<i>Anthropometric measures</i>			
BMI (kg/m^2)	27.4 (± 4.7)	38.9 (± 8.6)	<0.001*
Neck circumference (cm)	38 (± 2.4)	45 (± 5.1)	<0.001*
Waist circumference (cm)	97 (± 13.3)	121 (± 16.6)	<0.001*
<i>Clinical measures</i>			
SBP (mmHg)	124 (± 8.2)	130 (± 8.9)	0.039*
DBP (mmHg)	79 (± 6.9)	81 (± 6.7)	0.456
AHI (events/hour)	-	50 (± 27.8)	-
<i>Presence of chronic conditions</i>			
Hypertension	4 (21)	10 (55.6)	0.031*
Hypercholesterolemia	3 (15.8)	4 (16.7)	0.618
Diabetes	1 (5.3)	7 (38.9)	0.019*
Asthma	1 (5.3)	2 (11.1)	0.604
Depression	2 (10.5)	2 (11.1)	1.000

Anxiety	1 (5.3)	3 (16.7)	0.340
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<i>SF-36 questionnaire</i>			
SF-36 - 1	95 [10]	85 [37.5]	0.086
SF-36 - 2	87.5 [25]	100 [28.1]	0.743
SF-36 - 3	75 [50]	100 [81.3]	0.621
SF-36 - 4	80 [20]	80 [17.5]	0.483
SF-36 - 5	34.7 (\pm 8.4)	38.2 (\pm 7.3)	0.188
SF-36 - 6	100 [66.7]	100 [100]	0.688
SF-36 - 7	50 [15]	50 [13.8]	0.543
SF-36 - 8	72.6 (\pm 15.7)	65 (\pm 15.2)	0.142

Data are presented as mean (\pm SD), median [IQR], count (%).

Abbreviations: AHI: apnoea hypopnea index, BMI: body mass index; CON: control; DBP: diastolic blood pressure, OSA: obstructive sleep apnoea; SBP: systolic blood pressure. P values were determined using independent t-tests, Mann Whitney-U tests, or Chi-squared tests.

SF-36 questionnaire subscales as follows: 1: Limitations in physical activities because of health problems, 2: Limitations in social activities because of physical or emotional problems, 3: Limitations in usual role activities because of physical health problems, 4: Bodily pain, 5: General mental health (psychological distress and well-being), 6: Limitations in usual role activities because of emotional problems, 7: Vitality (energy and fatigue), 8: General health perceptions.

*Significance was accepted at $p \leq 0.050$.

3.2 Physical activity **profile of participants**

The physical activity characteristics of participants are reported in Table 2. None of these self-reported variables differed between the two groups. Based on the information derived from questionnaires, there was a higher presence of structural pain within the OSA group as compared to the CON. The majority of both the CON and OSA groups participated in some form of exercise, both in the past and at present. The mean total years of exercise between the groups were similar, however no significance could be noted due to the median result being utilized for non-parametric analysis. Furthermore, the number of participants in both groups exercising in the past and at present was similar, however, reported determinants for a noted reduction in PA within the past month in the CON group include time constraints, dark/unsafe environment, laziness, and covid restrictions. One of the participants within the CON group reported a chronic lung infection, which

resulted in them having a halt in exercise. Those from the OSA group that reported a reduction in exercise noted time constraints, covid, musculoskeletal injury and surgery. The injuries reported were in the shoulder and knee.

Table 2. Questionnaire-derived exercise profile of CON and OSA groups.

	CON group (N=19)	OSA group (N=18)	
Presence of structural pain	11 (57.9)	15 (83.3)	0.091
Past participation in exercise	14 (73.7)	13 (72.2)	1.000
Current participation in exercise	14 (73.7)	11 (61.1)	0.410
Pain aggravated by exercise	4 (36.4)	5 (33.3)	0.710
Total years of exercise	20 [44.9]	2 [25.2]	0.131
Questionnaire-derived self-reported exercise - days p/week	4 [3]	4 [4]	0.807
Questionnaire-derived self-reported exercise - min p/week	180 [390]	105 [420]	0.656
Seven-day diary-derived self-reported exercise - days p/week	3 [3]	3.5 [4]	0.855
Seven-day diary-derived self-reported exercise - min p/week	180 [380]	158 [301]	0.573
Those meeting ACSM exercise guidelines (>150 min/week)	12 (63.2)	12 (61)	0.898

Data are presented as count (%).median [IQR]

P values were determined using independent t-tests, Mann Whitney-U tests, or Chi-squared tests.

**Significance was accepted at $p \leq 0.050$.*

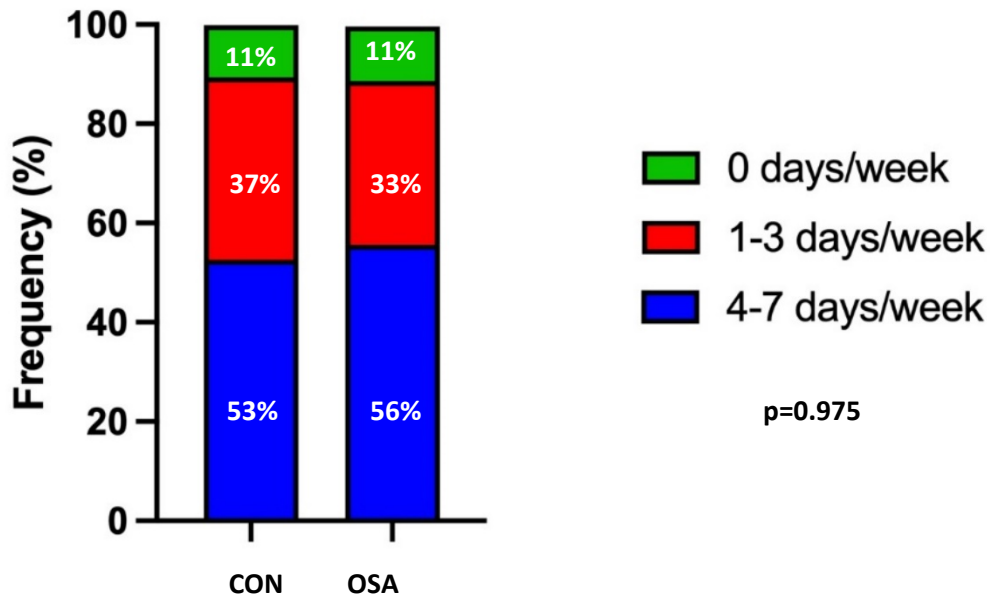


Figure 1. Comparison of current PA frequency between the CON (n=19), and OSA (n=18) groups as reported in the 7-day diary. CON: control group; OSA: obstructive sleep apnoea group. P-value represents between-group comparison as determined using a Chi-squared test.

Figure 1 shows the frequency of PA reported in the sleep diaries by participants in the OSA and CON groups. The distributions were not different between the two groups.

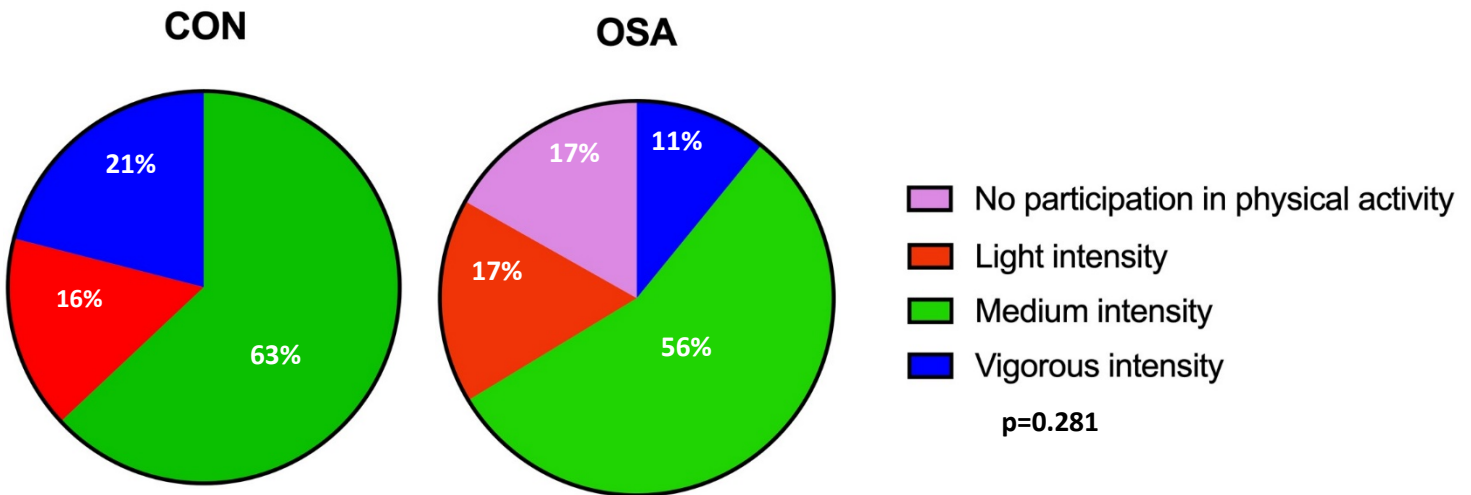


Figure 2. Comparison of PA intensity between the CON (n=19), and OSA (n=18) groups as reported in the questionnaire. CON: control group; OSA: obstructive sleep apnoea group. Light intensity was categorised as

1-3, medium intensity was categorized as 4-7, and vigorous intensity was categorized as 8-10. P-value represents between-group comparison as determined using a Chi-squared test.

The intensity of PA reported by the OSA and CON participants when they engaged in PA as per questionnaire as opposed to the sleep diary, are shown in Figure 2. This distribution was not different between the two groups. Of those who participated in PA exercise at a medium intensity was the most common.

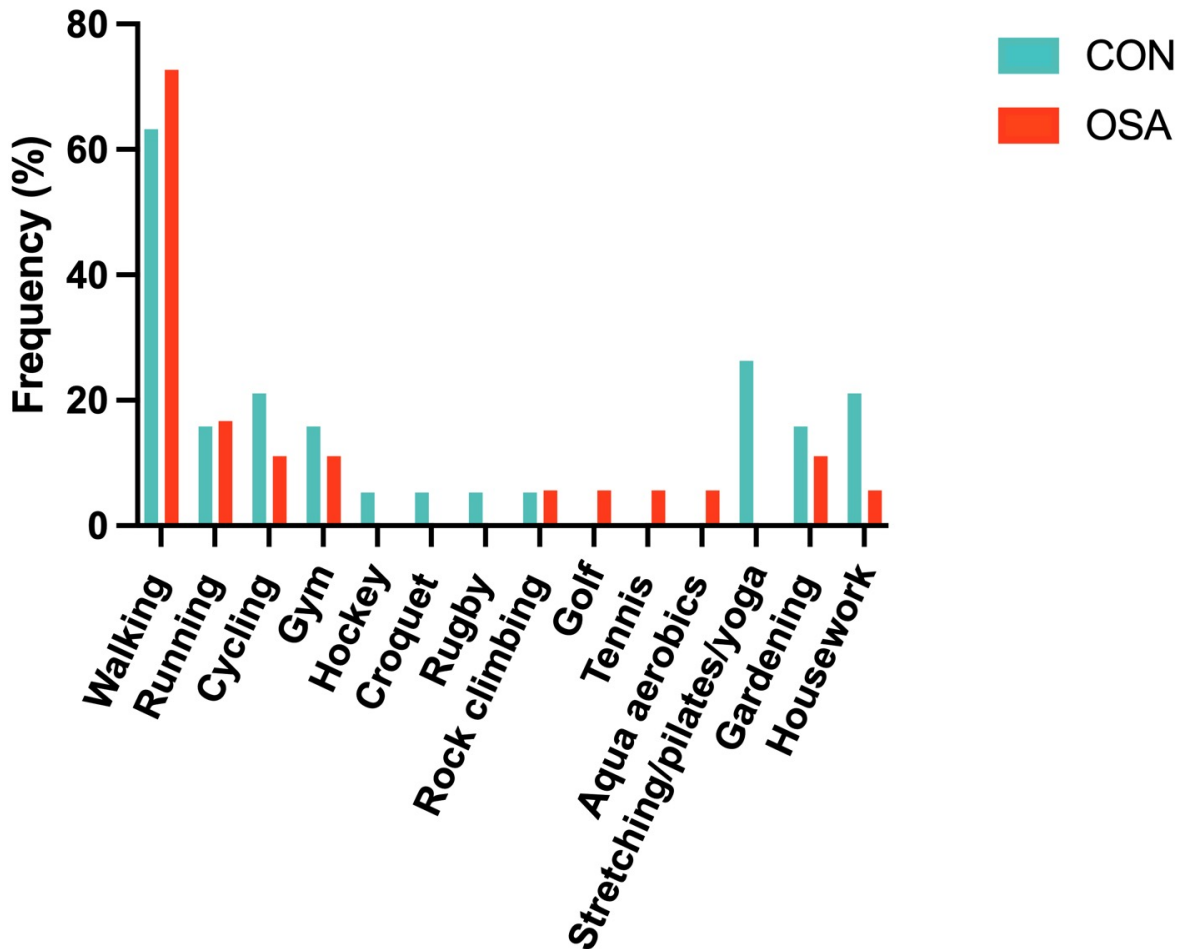


Figure 3. The preferred modes of PA engaged in by the CON (n=19) and OSA (n=18) groups as reported in the 7-day diary.

Figure 3 displays the types of physical activities carried out by the CON and OSA group participants during the week of monitoring. The most common form of activity reported within both groups was walking; (CON group: 63%, OSA group: 72%), but this distribution was not different between the two groups (p=0.556). Other forms of activity that were common among both groups was gardening (CON group: 16%, OSA group:

11%), housework (CON group: 21%, OSA group: 6%), cycling (CON group: 21%, OSA group: 11%), running (CON group: 16%, OSA group: 17%), and gym (CON group: 16%, OSA group: 11%), although also not different between the two groups ($p=0.677$, $p=0.412$, $p=0.942$, and $p=0.677$ respectively). Individuals from the OSA group had lower participation in sports-specific activities as less variety can be seen within the distribution of activities presented above. Those with OSA reported participation in tennis (OSA group: 5.6%), rock climbing (OSA group: 6%), and golf (OSA group: 6%), whereas those from the CON group had reports of participating in rock climbing (CON group: 6%), hockey (CON group: 5%), croquet (CON group: 5%), and rugby (CON group: 5%). Flexibility training (stretching, yoga) and Pilates, as a chosen activity, differed between the groups ($p=0.019$) as it was a common choice of activity in the CON group (26%) compared to zero reporting of this activity in the OSA group.

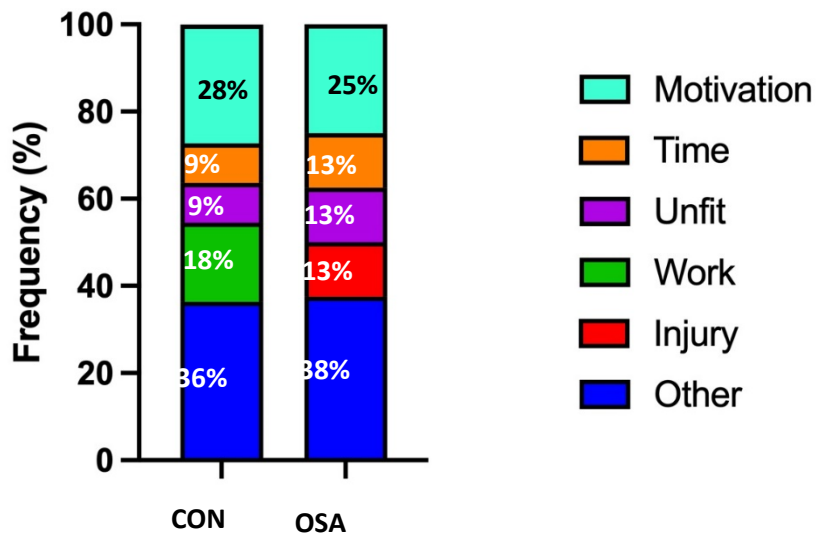


Figure 4. Comparison of current perceived barriers to exercise between the CON (n=19) and OSA (n=18) groups.

A higher proportion of the CON group (58%) identified the presence of a barrier that prevented them from participating in their desired PA, compared to the OSA group (44%, $p=0.413$). The barriers reported by both groups are presented in Figure 4. Of those who reported barriers to exercise, the most common barrier across both groups was noted as motivation (CON: 27%, OSA 25%, $p=1.000$). Other mutual barriers identified included time (CON: 9%, OSA 13%, $p=1.000$), and being unfit (CON: 9%, OSA 13%, $p=1.000$). Work was also perceived as a barrier by the CON (18%) but not the OSA group ($p=0.486$), while injury was present as a

barrier for the OSA (13%) but not the CON group ($p=0.486$). Just over two-thirds of both groups (CON: 36% and OSA: 38%) reported some “other” barrier, the specifics of which were unfortunately not identified.

4. DISCUSSION

The focus of this study was to understand the nature of current PA habits, perceptions, and barriers of individuals within an OSA cohort as compared to a CON group and make use of this information to design an exercise intervention framework for OSA patients. This framework is later, after further research including consideration of extension of the dataset, intended to be implemented in an under-resourced setting such as the public healthcare system in South Africa. Data were analysed from validated questionnaires to inform the design of the exercise intervention with the aim of reducing symptoms and severity of OSA. Published reviewed studies, mentioned above, support the efficacy of PA in reducing the severity of OSA, specifically AHI, associated symptoms – EDS, functional outcomes of sleep questionnaire, sleep health/parameters/stages, as well as overall CVD risk e.g. blood pressure, BMI. Within our study, participants within the OSA group had a significantly higher presence of self-reported chronic conditions ($p = 0.007$), including hypertension ($p = 0.031$) as well as diabetes ($p = 0.019$), when compared to the CON group. This aligns with several studies that have noted the high presence and association of chronic conditions with OSA, cardiometabolic in particular, which is likely linked to the build-up of oxidative stress derived from the activation of inflammatory mechanisms throughout arousals and relative hypoxias while sleeping (Lavie & Polotsky, 2009).

Although lower than the CON group (74%), current participation in PA within the OSA group was recorded as 61% of 18 individuals currently participating in PA. This decreased within the past month due to several reasons including time constraints due to job/familial demands, a dark/unsafe environment when they do find the time, laziness, covid restrictions which included the lack of facility access, illness/injury, and surgery which prevented them from taking part in PA, as well as a lack of interest. The presence of structural pain, including shoulder, lower back, knee, neck, hip, and wrist pain could be another reason for the halt in participation, as 33% of the OSA group reported that their pain is worsened/aggravated by exercise, but this finding was similar within the CON group with 36% reporting that exercise aggravates their injury/structural pain. Due to the high presence of structural pain that exists within our OSA sample (83%) compared to only 58% of the CON group reporting structural pain, as well as the fact that 33% experience pain aggravation

from exercise, programmes need to be carefully considered to avoid additional impact on the joints. Therefore, making use of existing exercise programme designs for obesity, including related musculoskeletal pain considerations are applicable within the framework proposed in this study. Being mindful of the presence and location of pain in the participants is essential when selecting the specific exercises to be included in the programme design and where possible, subtle adaptations may have to be considered on an individual basis.

From the 61% of individuals within the OSA group that are physically active, 50% reported frequent participation in exercise of four to seven days/week, with a median intensity of 6/10 on a range of 1 being 'very light, heart rate low, a sensation of "I could do this all day"', to 10 being 'vigorous, heart rate near max, a sensation of "I can't keep this up for too long"'. This would translate into exercise predominantly being of moderate intensity. It is important to note that the intensities presented in the questionnaire were not categorized into specific range measurements such as %HR, therefore intensity was scaled as a subjective measurement. This is a limitation as it allows for subjective differences in reported intensities and personal understanding of "light/moderate/vigorous" intensities. The high intensity reported by our participants suggests that either the tool used to assess intensity was imperfect, or that the participants perceive their activities to be more vigorous than what they truly are. According to ACSM, the guideline for PA recommends at least 180 minutes/week of moderate-vigorous intensity exercise (American College of Sports Medicine, 2017). Of the CON group, 63% met this guideline, and 61% of the OSA group met this guideline. This encourages the inclusion of PA into the intervention design, as guidelines need to be met in order to see a reduction in inflammation and an overall increase in health parameters (American College of Sports Medicine, 2017).

Barrow *et al.* (2019) noted that the greatest amount of weight loss and reduced body/fat mass was achieved with high-intensity exercises in obese individuals with OSA. Vigorous intensities of 70-80% HRmax were found to optimize weight management and improved physical function which in turn was also shown to improve pain and function in these individuals. It is important to mention that vigorous exercise prescription may require pre-participation screening depending on the patient's risk profile. Most of the exercises presented in the literature review (chapter 1) were performed three times per week, at durations of 20-90 minutes. Seeing that those within the OSA group are currently active for four to seven days/week, following ACSM guidelines (Donnelly *et al.*, 2009) along with suggested studies of evidence-based improvements, it is recommended that the programme design incorporate training for three to five days/week with durations of

30-60 minutes per session, to target long term weight loss guidelines of 200-300 min/week of PA (Donnelly *et al.*, 2009) Chosen exercises for the anticipated programme design can be incorporated into a moderate intensity training regime, but where safe, consideration can be given to progression to a high-intensity training regime as reductions in systolic blood pressure and waist circumference was also noted with high-intensity training by Way *et al.* (2020).

Of those who participate in PA, in our study, most of the individuals across both groups preferred walking, with 53% of those with OSA indicating that this was their preferred activity, similar to the CON group whereby 32% preferred walking. Other activities such as running (12%), gym (8%), gardening (8%), and cycling (8%) were also among those that were preferred by the OSA group. A study by Evans *et al.* (2017) tasked participants with completing six tests which included incremental speed tests on a treadmill and power tests on a cycle ergometer to assess the effects of exercise modality/intensity on energy expenditure (EE) and cardiovascular response. All individuals were on CPAP treatment, and were obese (BMI > 30kg/m²). Peak oxygen uptake ($\dot{V}O_2$ peak), peak ventilation (VE) and heart rate (HR) achieved on the treadmill were higher than the cycle ergometer. The total EE was four times greater with the treadmill effort than with the cycle ergometer at a vigorous intensity (80% $\dot{V}O_2$ peak), and three times greater with moderate intensity (60% $\dot{V}O_2$ peak). There was also a higher reported breathlessness, measured with the Borg category scale, for those who participated in the cycling. The absolute aerobic capacity for cycling was 68%, whereas the treadmill was at 85%. This means that at a matched intensity, the attainable total energy expenditure is greater in walking than in cycling, suggesting that incorporating treadmill exercises into a programme will be beneficial, as participants were shown to sustain walking for longer at a matched intensity. Considering the economic status of the average South African, as well as their accessibility to equipment, including the activity of walking into an exercise intervention for cardiovascular training as part of their activities of daily living should be an effective means at reducing OSA symptoms and the risk of associated secondary conditions. As noted by the high preference for walking as a chosen activity within our OSA sample, the issue of compliance is not expected to be a factor, and considering that participants in the study by Evans *et al.* (2017) have been shown to sustain walking for longer periods than cycling, including walking into the programme design is considered ideal.

Andrade *et al.* (2016) noted that endurance exercise resulted in upper airway muscle activation thereby opposing pharyngeal collapse during sleep. This finding supports the notion to include endurance activities into the designed programme, such as longer walks (+20 minutes) at an intensity of 40-70% HRR which

includes moderate, and the lower range of high intensity. Ranges for HRR as followed by the Karvonen formula are defined as: light intensity exercise = 30-40% HRR, moderate intensity exercise = 40-60% HRR, vigorous intensity exercise = 60-90% HRR (Ignaszewski *et al.*, 2017).

It is however important to note that as little as 10 minutes of aerobic activity (walking) per day infers a clinical benefit (American College of Sports Medicine, 2000). A significant association between hypertension and the presence of OSA ($p=0.031$) was noted with 56% of the OSA population having self-reported hypertension. Treadmill walking has been shown to result in improvement in systolic blood pressure, along with an increase in fat oxidation (Colpitts *et al.*, 2021). Regular moderate-intensity aerobic exercise can also improve insulin sensitivity and glycaemic control by reducing lipid hydroperoxides, in turn decreasing oxidative stress (Ceriello & Motz, 2004). Aerobic training, in the form of walking, showed a significant improvement in absolute $\dot{V}O_2$ max values (Aksović *et al.*, 2020), and the choice of walking as a PA can be prescribed to individuals with less chance of injury as no supervision is required. Significant effects on cardio-respiratory fitness were also noted (Aksović *et al.*, 2020). Aerobic training, consisting of moderate-intensity treadmill training at 60% HRR, also resulted in a decrease in AHI/ODI (Kline *et al.*, 2011), thereby supporting the choice of using walking as an aerobic/cardiovascular activity to include in the designed programme.

When assessing health behaviours in a population, it is important to understand the participants' behaviour at the present moment, as well as the factors that can contribute to a change in their behaviour. Making use of the COM-B model for behaviour change, we can analyse three components that will contribute to change – capability (C): the individual's psychological and physical ability to participate in the activity, opportunity (O): external factors which may contribute to making this change a possibility, and motivation (M): the individual's conscious and unconscious cognitive processes which can influence behaviour. (Barker *et al.*, 2016). This model considers that an individual's behaviour can only change if the person has the capability and opportunity to engage in the planned changed behaviour. While capability can refer to the individuals' ability to participate in PA for example, it can also be used as a step in understanding their barriers to PA as it analyses their mental state, knowledge and skills, and their physical strength. The physical opportunities provided by the environment can also be analysed from a barrier point of view - if the environment to perform PA does not feel safe, this can lower the likelihood of being physically active in that space. Lastly, in order to benefit from PA, the individual needs to turn the desired behaviour into something that they want to do, rather than keeping it at something that they need to do. "The more capable an individual is, or believes

they are, of enacting a behaviour change, and the more conducive the environment is to enacting it, the more they will tend to want it” (West & Michie, 2020).

A lack of participation in PA could be due to barriers ranging from environmental factors to psychological factors. Some individuals may state poor health, too little time, being overweight or lack of exercise gear as a barrier. Skaal (2011) analysed the presence of barriers to PA in South African healthcare workers, and categorized their barriers into family support, environment (hospital and home access), and motivation. Lack of family support was reported by 51% of the medical staff, and motivation as a factor was reported by 82.5% of staff irrespective of age, gender and job category. Skaal (2011) highlights the “need to introduce cost-effective exercise programs to minimize barriers”, and states that cultural beliefs could also be perceived as a barrier to exercise, therefore an intervention design should consider the culture of South Africa in the design, to ensure all aspects have been accommodated in order to make a long-term impact. Environmental factors were also seen as a barrier by 45% of the hospital staff, as they reported their homes were not conducive to exercise.

Within this study, individuals with OSA reported that ‘motivation’ (25%) and ‘other’ (38%) were the top-ranking barriers that prevented them from participating in exercise. Other barriers included ‘time’ (12.5%), ‘being unfit’ (12.5%), and ‘injury’ (12.5%). This was similar in the CON group, however, ‘injury’ was not reported as a barrier, while 18% reported the presence of ‘work’ as a barrier, which in turn was not seen in the OSA individuals. Biddle *et al.* (2011) found, in a randomized control trial, that sports games had physiological, cardiovascular, and muscle strength benefits. In view of the observation that both the OSA and CON groups reported “motivation” as a barrier (25% and 27% respectively), involvement in a group sport setting or exercise setting may allow individuals the opportunity to participate in PA while receiving the social motivation that is commonly perceived as a barrier in their everyday life. Supervised exercise classes might hence be of value, and will provide the opportunity, if delivered by an individual formally trained in exercise prescription, to overcome the barrier of injury affecting participation in exercise for those who feel they do not know how to modify their exercise routine in order to minimize pain.

Finding ways of introducing PA into our daily lives is an important step on the journey to a healthy lifestyle. Workspaces should be designed in a way that allows for the employees to remain physically active throughout the day such as reminders on the benefits of taking the stairs instead of the elevators, and

workspaces set up with wireless phones to ensure employees have the ability to stand up and walk around the office space while on the phone. Being physically active throughout the day is important to maintain a healthy lifestyle and reduce your mortality risk (Wen *et al.*, 2011); this can include activities of daily living such as gardening, cleaning the house, making use of walking as a tool of navigating around, and hanging the laundry. While PA can be viewed as a path to attaining longer life expectancy and reducing the risk of disease, the benefits of social value it provides should also be considered in order to promote the concept of “leisure” PA. General recommendations for PA can include group settings within the public space such as outdoor group activities or park runs for instance which integrate culture and community (Silva *et al.*, 2017).

There was some degree of interest in sports-specific activities noted in the OSA group i.e. rock climbing (6%), aqua aerobics (6%), tennis (6%), and golf (6%). Donnelly *et al.* (2009) concluded that sedentary individuals, of the general population, could perform ~80 minutes/day of moderate intensity PA or 35 minutes/day of vigorous PA to prevent weight gain. Due to the presence of ‘time’ and ‘motivation’ as a barrier to exercise within both groups, as well as reports of “getting bored” as a reason of stopped participation in exercise, shorter sessions that consist of sport-specific activities are recommended for the programme design.

According to ACSM guidelines, the promotion and maintenance of good health and physical independence can be achieved by participation in activities that increase muscular strength (i.e. resistance training) for at least two days a week, while eight to ten exercises performed on two or more nonconsecutive days that make use of the major muscle groups with 8-12 repetitions of each is recommended (Haskell *et al.*, 2007). Individuals with OSA within the sample for our study had a mean (\pm SD) BMI of 38.9kg/m^2 (± 8.6) which categorizes the OSA group as obese. The benefit, reviewed by Donnelly *et al.* (2009), of including resistance training into the programme design, as opposed to purely aerobic training, provides those with OSA the opportunity to target a reduction in the health risks associated with OSA such as hypertension, CVD, and diabetes, which are represented in our OSA sample, by increasing fat-free mass and increasing loss of fat mass associated with a reduction in health risk.

A supervised programme consisting of shoulder presses, latissimus dorsi pull downs, leg extensions, leg flexions, chest presses, upright rows, leg presses, bicep curls, tricep extensions, and abdominal crunches was followed by Kline *et al.* (2011) to also yield a reduction in AHI/ODI. Exercises were followed for 10-12 reps, with a repetition for two sets. Mendham *et al.* (2021) made use of a 12-week intervention for obese females,

from South Africa, consisting of similar exercises i.e. squats, lunges, bicep curls, push-ups, and shoulder presses at 60-70% peak HR, which led to decreased body weight, increased insulin sensitivity, increased peak oxygen consumption, decreased BMI and a decreased hip/waist ratio was observed in the participants. While these are broad guidelines, more specific exercises can be tailored depending on the participants taking age, injuries, comorbidities as well as their exercise setting into account. It is also evident that while it is preferable that these activities become part of daily life, a minimum duration of 2 to 3 months is preferred, but the longer the programme is adhered to, the greater the health benefits.

Of interest is the co-muscular activation between the gastrocnemius muscle and the genioglossus muscle observed in dogs by Haxhiu *et al.* (1984) and Hussain *et al.* (1991) indicated that including lower body exercises in the designed programme could be beneficial for the reduction of airway resistance, thereby reducing the severity of OSA symptoms. Bughin *et al.* (2020) also noted the benefit of resistance training on sleep parameters, such as a decrease in AHI during REM sleep throughout an eight-week intervention which reduced the cardiometabolic consequences of OSA. Collins *et al.*, (2021) found a reduction in fat mass and hip circumference in an intervention designed to include both aerobic activities as well as resistance activities. The benefits of resistance training on the physiological parameters, linked to chronic disease and OSA severity, indicate that the inclusion of resistance training accompanying aerobic training will be beneficial in the programme design.

Along with exercise prescription, patient education surrounding the role of sleep, ways to target sleep hygiene, OSA, the consequences thereof, and disease management will be beneficial. Even though only 11% of the OSA group indicated that they are smokers, 33% indicated that they are regular alcohol consumers, and therefore a change in lifestyle habits can also be advocated. The eight-week intervention followed by Bughin *et al.* (2020) included such educational sessions. Due to the suppressant nature of alcohol, consumption of alcohol can increase the number of apnoeas in patients with OSA. This is due to suppression in the activity of upper airway dilator muscles in comparison to the diaphragm, thereby increasing airway resistance (Mittler *et al.*, 1988). Findings such as these should be raised in the educational sessions. Although no individuals within our sample indicated a “lack of knowledge” as a barrier to PA participation, from a clinically ethical standpoint it would be imperative to provide patient education along with lifestyle modification suggestions on all fronts and contribute to the holistic approach.

A framework that follows the points mentioned above, taking into consideration the environmental limitations, should aim to show improvements in cardiorespiratory function, muscle cross-sectional area and strength, physical function, sleep parameters such as AHI, ODI and daytime sleepiness, reductions in body weight, visceral adiposity i.e. waist and neck circumference, as well as better insulin sensitivity profile and blood pressures. The framework is to be developed in three stages, following an outline by the South African Medical Research Council (MRC):

Stage 1

The “gap analysis” aims to identify and summarise aspects of previous intervention designs for individuals with OSA, that require contextual adaptations. A brief literature review of existing literature and studies was performed to cover interventions targeted to effect a reduction in the severity/symptoms of OSA, as well as those targeted to bring about a reduction of chronic conditions in individuals. The benefits highlighted, as well as the exercise intervention specifics such as frequency, intensity, type of exercise, and duration of sessions can then be used as a baseline for the intervention design.

Stage 2

Semi-structured interviews and questionnaires, which were conducted within the previous study (HREC Ref: 142/2021), were analysed to derive an understanding of the nature of, and perception of, current PA habits as well as barriers to exercise faced by individuals with OSA. Barriers, exercise/PA frequency, and exercise intensities were thematically organized and used to make decisions on the content of the proposed framework. Following the MRC guidelines, the components to cover in the framework include the type of PA sessions, parameters of the session (e.g., frequency, intensity, type of activity, duration of the session), and methods of organizing and delivering these sessions (e.g. type of practitioner, setting, and location) (Medical Research Council, 2000).

Stage 3

The project team drafted the first document for submission. Pilot studies, with the designed intervention, are proposed to be carried out to evaluate the impact on the severity of OSA with a special focus on those with OSA with limited access to healthcare. The pilot intervention will allow for the refinement and adaptation of the programme with the aim of improving the efficacy, availability, adherence and benefits of

the proposed intervention. It will allow stakeholder feedback from all the different members involved such as the OSA participants themselves, the medical personnel (biokineticists, nurses, doctors) and the administration staff involved in the implantation of the pilot and then the longer-term exercise program. This will provide a basis for an understanding of the feasibility of the intervention. Criteria to be considered would include (1) an acceptable intervention design (content and delivery), (2) adherence of OSA individuals at the sleep clinic to the intervention, (3) analysis of cost-effectiveness, and (4) capacity of those providing the intervention to deliver as planned (Medical Research Council, 2000). There are various ways to design an intervention depending on whom it is targeted i.e. at the level of individual patient care, at the level of an organizational or service modification, an intervention targeted to the health professional, or an intervention delivered at a population level. In the case of this study, all four sectors will be approached; (1) the intervention is designed to target individuals who have OSA (individual patient care), (2) to adapt the treatment model, used in a tertiary public health sector hospital to include PA and exercise as an option of a modality of treatment (organizational modification with the introduction of a biokineticist into OSA primary care services), (3) while increasing awareness around the sleeping disorder in healthcare workers of the community (targeted toward the healthcare professional), and (4) intending the intervention to be delivered at a later stage at a population level, to those from resource limited settings.

From a broad perspective, the phases to cover in the framework, according to MRC guidelines are (1) pre-clinical/theoretical, (2) phase I/modeling, (3) phase II/exploratory trials, (4) phase III/main trial, and (5) phase IV/long term surveillance (Medical Research Council, 2000). Within this study, we have completed the preclinical/theoretical phase, as well as the modeling phase. The theoretical component incorporates exploring relevant theory to ensure the best choice of intervention, as well as hypothesizing and predicting major confounders and strategic design issues – this phase included completing a literature review on the benefits of PA interventions for health, weight loss, chronic conditions, and OSA severity. The benefits of PA regarding OSA can be grouped according to benefits in the treatment of obesity, which is a risk factor of OSA, benefits on sleep parameters of individuals with OSA, benefit on skeletal parameters, and benefit for CVD parameters. Peak $\dot{V}O_2$, leg strength, HDL, fat-free mass, fat oxidation, and telomere length were all shown to increase with participation in PA across various studies analysed in the literature review above (see Chapter 1). Improvement in telomere length is beneficial as telomeres are protective protein complexes which limit the chromosome shortening caused by replication; a shortened telomere has been correlated with metabolic disorders, while telomere lengthening is correlated with longevity (Brandao *et al.*, 2020). Improvements in pulse wave velocity, systolic blood pressure, triglycerides, lipid profiles, brachial artery-flow mediated

dilation, hip/waist ratio, physical functioning, physical health, and emotional health were also noted (See Chapter 1). Reductions in AHI, ODI, and EDS were noted in individuals with OSA who had undergone exercise interventions, and an increase in stage N3 sleep was also noted in many studies (see Chapter 1).

The semi-structured interviews and questionnaires which were completed provided the opportunity to contextualize the problem by understanding the population and the individual's perspective of PA, their participation in it, and their identified barriers towards it. There was a high presence of indicated "barriers" within the OSA group (67%), indicating that there are possibilities to have higher performance in PA if barriers were to be removed. The most commonly identified barrier was "motivation", and therefore the creation of an intervention that can incorporate PA within a treatment plan, especially if this can be performed in a group setting, will counteract the barrier as the health professional team shall aim to create spaces of motivation for those with OSA to be physically active. The identification of "time" as a barrier indicates that the programme design cannot be too long, otherwise individuals may feel restricted in partaking. Therefore, a suggestion of shorter more frequent sessions is advised. The inclusion of two short sessions in one day is another consideration. The identification of "injury" as a barrier further indicates the need for supervised programmes to be designed by a biokineticist, as injury-preventative individualized programmes which work with the current injury in mind, can be devised; understanding this will reduce the risk of further injury to these individuals, and encourage participation in PA without fear-avoidant behavior. This assists in phase I (modeling) of the intervention framework design, as components of the intervention can be identified in a context-specific environment, to decipher what the underlying mechanisms that influence the outcomes would be.

Based on the literature, and the qualitative research received from our participants, the proposed framework should include an exercise intervention that follows a FITT (frequency, intensity, type of activity, time of session) principle that considers a moderate frequency of three to five times/week, with a medium and-building-up-to a higher intensity of 40-80% HRR. Considering the high risk that these individuals with OSA would be (hypertension, diabetes, metabolic syndrome etc.) it is most advised from a clinical perspective to advocate for moderate intensity as opposed to vigorous intensity. Vigorous intensity would need supervision, and since ADL (PA) and home based intervention are to be encouraged in the framework, an intensity that does not require supervision is advised for safety purposes. Shorter sessions of 25-40 minutes per session are advised, but building up to 60 minutes where possible, and inclusion of aerobic and resistance exercises with a focus on walking as well as lower body activities. Suggested group sessions should be considered.

Table 3. Proposed framework for an exercise intervention in the treatment of OSA severity symptoms; developed based on data received from questionnaires/diaries used in this study, and a review of existing literatures (as per the FITT principles).

	Frequency	Intensity	Type	Time
Aerobic	3-5 times/week	40-80% HRR *RPE of 12-15 on the Borg Scale	<ul style="list-style-type: none"> ○ Focus on walking on a treadmill/outdoor field ○ Group walks are recommended 	20-40 minutes/session
Resistance	2-3 times/week (not consecutively)	RPE of 12-15 on the Borg Scale (Medium intensity)	<ul style="list-style-type: none"> ○ Focus on lower limb activations ○ Also include upper body exercises** ○ Guided by facilities and equipment availability – body weight, therabands, weights or machines 	20-30 minutes/session
Flexibility	3-4 times/week	RPE of 9-12 on the Borg Scale	<ul style="list-style-type: none"> ○ Pilates ○ Yoga ○ Stretching 	+20 minutes/session
Additional activities	1-2 times/week	RPE of 7-9 on the Borg Scale	<ul style="list-style-type: none"> ○ Breathing exercises ○ Oropharyngeal movements 	10 minutes/session

Special considerations to note:

- **RPE can be used where heart rate targets cannot be monitored.*
- ***Avoid overhead activities at high resistance (contraindication for hypertensive individuals).*
- *Check blood sugar levels before the commencement of exercise for diabetic individuals (safe range is between 5.0 and 13.9 mmol/L) (Colberg et al., 2016).*
- *Pre-participation screening is necessary in higher risk individuals: individualization of programs where indicated.*
- *Higher risk individuals such as those with heart failure may require lower intensities and may start at a HRR of <40% with much shorter exercise intervals.*

-
- *Higher risk individuals are to access these programs at secondary and tertiary hospital levels where more advanced monitoring and clinical management facilities are available.*
 - *Duration of program: aim to make the program a lifestyle adaptation.*
-

To follow, an exploratory trial should be run for phase II which will allow for a replicable intervention and feasible exercise protocol, to target OSA severity, to be designed based on the suggestions above, one that is contextually specific to the target population in terms of frequency, intensity, mode of exercise, and sessional deliverance given the environmental and economical constraints; this would be referred to as the pilot trial. This pilot trial can then lead to the definitive randomized control trial that will be aimed at being trialed at a tertiary hospital in phase III, to investigate the benefit of the exercise intervention on a group of South African individuals from a low-income setting, that have OSA. Stage IV, long-term implementation, would then need to be administered and assessed, to determine if the exercise intervention can reliably be replicated in an uncontrolled setting over the long term. (Medical Research Council, 2000)

Limitations to this study include the sample participants that were selected in the parent study, as well as the sample size. From an economic status perspective, the individuals analysed in this study are from a middle-income setting, as opposed to the desired low-income setting. It is also important to note that all OSA participants in this study were on CPAP treatment, which may affect many of the outcome measures and behavioural tendencies. Time since AHI diagnosis might have also had an influence on the results related to physical activity, due to the long-term impacts that OSA has regarding the increased risk for cardiovascular, cerebrovascular and metabolic syndrome disorders, and should therefore have been considered. It is necessary to expand the OSA cohort to include those currently not on CPAP treatment, and individuals from more challenging socioeconomic circumstances, to ensure the framework considers the diversity within our healthcare systems. The intended pilot studies could not be carried out on participants due to COVID restrictions and accessibility, therefore, needing this to be carried out at a later stage. It is suggested that the pilot studies be carried out in a more low-income setting.

5. CONCLUSION

By making use of custom and validated questionnaires, past and current PA habits, preferences, and barriers of OSA patients were learnt. Detailed diaries provided specifics on the preferred mode of PA and exercise, preferred frequency, intensity, and duration of sessions over the course of one week. This information was

used, alongside validated exercise interventions reviewed in chapter 1, to design an exercise intervention framework for OSA patients, one that can be implemented in an under-resourced setting. The proposed exercise intervention framework derived from this study includes a moderate frequency of three to five times/week, a medium building up to a high intensity of 40-80% HRR, shorter sessions of 25-40 minutes per session building up to 60 minutes where possible, with an inclusion of aerobic, flexibility, and resistance exercises with a focus on walking. Suggested group sessions should be considered. There should also be a focus on the encouragement to increase participation in overall PA, such as daily living activities including and not limited to housework, daily commute by walking, and community-based group sessions.

For future research, we recommend stages II, III, and IV of this framework design be carried out to allow for the creation of a reviewed and evaluated exercise programme; one that can be incorporated into a treatment protocol to be used in a tertiary public health sector hospital. A methodological approach to framework design, as stated above, could provide an inexpensive and accessible holistic treatment option to those diagnosed with OSA, from a low-income setting, within South Africa.

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APPENDICES

Appendix A – Participant questionnaire

Physical activity and sedentary behaviour among patients with obstructive sleep apnoea in South Africa

PARTICIPANT CONTACT INFORMATION

Participant code: _____

Date: _____

PARTICIPANT DETAILS

First name: _____

Surname: _____

Postal address: _____

_____ Code: _____

Email address: _____

Phone number (h): _____ Cell phone: _____

EMERGENCY CONTACT

Please give us the contact details of someone we may call in case of an emergency.

Name: _____ Relation: _____

Cell phone: _____ Landline: _____

Physical activity and sedentary behaviour among patients with obstructive sleep apnoea in South Africa

GENERAL QUESTIONNAIRE

Participant code: _____

Date: _____

PARTICIPANT DETAILS

Date of birth: _____

Age: _____

Gender: _____

MEDICAL HISTORY AND HEALTH

Do you currently suffer from **any chronic medical condition**? Yes No

If **yes**, please list the condition(s):

Name of condition	Person who diagnosed	Date diagnosed

Do you currently use any **chronic medication(s)**? Yes No

If **yes**, please list the medication(s):

Name of medication	Purpose	Years taken

Have you ever been **diagnosed** with **sleep apnoea**? Yes No

If **yes**, please provide the following information:

When was the diagnosis made? _____ mm/yy

How was the diagnosis made? _____

What was your **apnoea/hypopnoea index**? _____ AHI

Are you currently being treated for **sleep apnoea**? Yes No

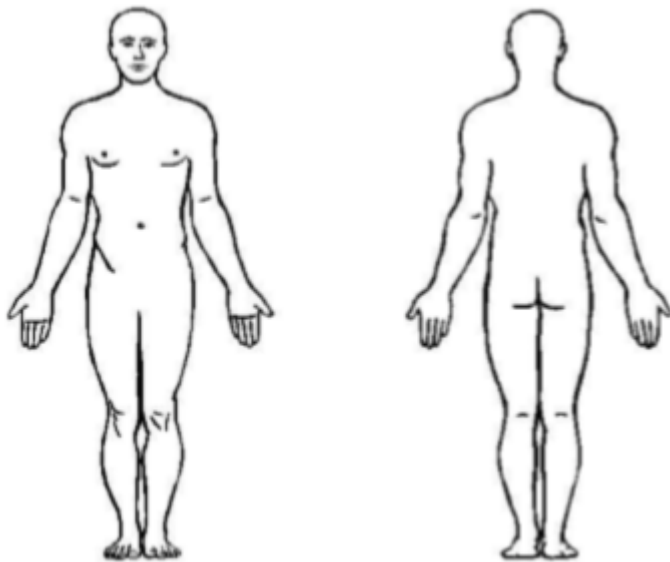
If **yes**, please describe your **treatment**: _____

Do you **snore loudly** (louder than talking or loud enough to be heard through closed doors)?
Yes No

Do you often feel **tired, fatigued, or sleepy** during the daytime, even after a "good" night's sleep?
Yes No

Has anyone has ever observed you **stop breathing** during your sleep? Yes No

Please indicate on the figures below any aches, pains or problem areas.



Please give details of any areas indicated: _____

Are any of these injuries aggravated by exercise? Yes No

Are you currently receiving treatment for any structural problem? Yes No

If yes, please describe: _____

For women only:

Are you currently **pregnant** or have you **given birth** in the last 6 months? Yes No

Are you currently breast feeding? Yes No

Are you:

Pre-menopausal

Menopausal

Post-menopausal

SF36 Questionnaire

INSTRUCTIONS

Please answer every question. Some questions may look like others, but each one is different. Please take the time to read and answer each question carefully by **circling** the number that best represents your response. Please respond to each line within each question.

1. In general, would you say your **health** is?

Excellent	Very Good	Good	Fair	Poor
1	2	3	4	5

2. **Compared to one year ago**, how would you rate your health in general **now**?

Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago
1	2	3	4	5

3. The following questions are about **activities** you might do during a **typical day**. Does your **health** now **limit** you in these activities? If so, **how much**?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
--	---------------------------	------------------------------	--------------------------------------

A. Vigorous activities , such as running, lifting heavy objects participating in strenuous sports	1	2	3
B. Moderate activities , such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	1	2	3
C. Lifting or carrying groceries	1	2	3
D. Climbing several flights of stairs	1	2	3
E. Climbing one flight of stairs	1	2	3
F. Bending, kneeling, or stooping	1	2	3
G. Walking more than a mile	1	2	3
H. Walking several hundred yards	1	2	3
I. Walking one hundred yards	1	2	3
J. Bathing or dressing yourself	1	2	3

4. During the **past 4 weeks**, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your **physical health**?

	All the time	Most of the time	Some of the time	A little of the time	None of the time
A. Cut down on the amount of time you spend on work or other activities	1	2	3	4	5
B. Accomplished less than you would like	1	2	3	4	5
C. Were limited in the kind of work or other activities	1	2	3	4	5
D. Had difficulty performing the work or other activities (for example, it took extra effort)	1	2	3	4	5

5. During the **past 4 weeks**, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any **emotional problems** (such as feeling depressed or anxious)?

	All the time	Most of the time	Some of the time	A little of the time	None of the time
A. Cut down on the amount of time you spend on work or other activities	1	2	3	4	5
B. Accomplished less than you would like	1	2	3	4	5
C. Did work or activities less carefully than usual	1	2	3	4	5

6. During the **past 4 weeks**, to what extent has your **physical health** or **emotional problems** interfered with your **social activities** with family, friends, neighbours, or groups?

Not at all	Slightly	Moderately	Quite a bit	Extremely
1	2	3	4	5

7. How much **bodily pain** have you had during the **past 4 weeks**?

None	Very mild	Mild	Moderate	Severe	Very severe
1	2	3	4	5	6

8. During the **past 4 weeks**, how much did **pain interfere** with your **normal work** (including both work outside the home and housework)?

Not at all	Slightly	Moderately	Quite a bit	Extremely
1	2	3	4	5

9. These questions are about how you **feel** and how things have been with you during the **past 4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks...

	All the time	Most of the time	Some of the time	A little of the time	None of the time
A. did you feel full of life?	1	2	3	4	5
B. have you been very nervous?	1	2	3	4	5
C. have you felt so down in the dumps nothing could cheer you up?	1	2	3	4	5
D. have you felt calm and peaceful?	1	2	3	4	5
E. did you have a lot of energy?	1	2	3	4	5
F. have you felt downhearted and depressed?	1	2	3	4	5
G. did you feel worn out?	1	2	3	4	5
H. have you been happy?	1	2	3	4	5
I. did you feel tired?	1	2	3	4	5

10. During the **past 4 weeks**, how much of the time has your **physical health** or **emotional problems** **interfered** with your **social** activities (like visiting friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
1	2	3	4	5

11. How **TRUE** or **FALSE** is each of the following statements for you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false

A. I seem to get sick a little easier than other people	1	2	3	4	5
B. I am as healthy as anybody I know	1	2	3	4	5
C. I expect my health to get worse	1	2	3	4	5
D. My health is excellent	1	2	3	4	5

PHYSICAL ACTIVITY

Do you **currently** (past month) participate in **regular physical activity**? Yes No

If **yes**, please provide the following details:

What **type(s)** of exercise do you do in a usual week? _____

For how many **years** have you been exercising? _____ Years

On how many **days per week** do you exercise? _____ d/week

For how many **hours per week** do you exercise? _____ h/week

On a scale of 1 to 10, how would you rate the average **intensity** of your exercise sessions?

1 _____ 10

Intensity:	Very light	Moderate	Vigorous
Heart rate:	Low		Near max
Sensation:	“I could do this all day “		“I can’t keep this up for long”

If you **do not currently** exercise, did you exercise in the past? Yes No

If yes, please provide the following details:

How **long ago** did you stop exercising? _____ Years

Why did you **stop** exercising? _____

What **type(s)** of exercise did you used to do in a usual week? _____

On how many **days per week** did you used to exercise? _____d/week

For how many **hours per week** did you used to exercise? _____ h/week

On a scale of 1 to 10, how would you rate the average **intensity** of your past exercise sessions?

1 _____ 10

Intensity:	Very light	Moderate	Vigorous
Heart rate:	Low		Near max
Sensation:	“I could do this all day “		“ I can’t keep this up for long”

Do you have any **condition or reason** for **not** being able to **move about** or **participate in physical activity** should you choose? Yes No

If **yes**, please describe: _____

Do you need to make use of any **aid to move about** (e.g. cane, brace, wheelchair)? Yes No

If **yes**, please describe: _____

On a scale of 1 to 10, how **satisfied** are you with your current physical activity habits?

1 _____ 10

Satisfaction:	Not at all	Somewhat	Very
----------------------	------------	----------	------

What would you say are the **main barriers** preventing you from exercising? (you may choose more than one)

- Lack of facilities
- No motivation

- No time
- Injury/illness

- Unfit
- Appearance
- Lack of knowledge

- Family
- Work

OTHER LIFESTYLE FACTORS

On a scale of 1-10 (with 1 being poor and 10 being excellent), how would you assess the **quality** of your **eating habits**?

1 _____ 10

Quality:	Very poor	Moderate	Excellent
-----------------	-----------	----------	-----------

Which of these best describes your **smoking status** (any tobacco)?

- Smoker: Has smoked cigarettes regularly (at least 1 per day) for at least 1 year
- Occasional: Smokes, but not regularly
- Ex-smoker: Stopped for at least 1 year after smoking regularly
- Non-user: Never smoked regularly

If you are a **current smoker**, how **many** cigarettes do you smoke **per day**? _____ No/day

If you are an **ex-smoker**, how **many** cigarettes did you smoke **per day**? _____ No/day

Which of these best describes your **alcohol use**?

- Consumes alcohol: Has consumed alcohol (at least 1 per week) for at least 1 year
- Ex-consumer: Consumed alcohol in the past but has not used alcohol for at least 1 year
- Non-consumer: Has never consumed alcohol regularly

If you **currently consume alcohol**, how many **drinks** do you have in an average **week**?

_____ No/week

HOME ENVIRONMENT, EDUCATION AND OCCUPATION

How many people (adults and children) usually live in your home (including yourself)? _____

How **many rooms** does your home have this includes bedrooms, bathrooms, kitchen lounge etc)?
_____ No of rooms

Does the **household** or any member of the household (including yourself) **own or have** any of the following? (Include only if they are in working condition)

- | | |
|--|--|
| <input type="checkbox"/> Electric iron | <input type="checkbox"/> Sofa |
| <input type="checkbox"/> Refrigerator | <input type="checkbox"/> Radio or CD player |
| <input type="checkbox"/> Television | <input type="checkbox"/> Telephone(landline) |
| <input type="checkbox"/> Satellite Dish or Cable Television | <input type="checkbox"/> Cell phone |
| <input type="checkbox"/> DVD player or VCR | <input type="checkbox"/> Fan |
| <input type="checkbox"/> Computer (only include a computer purchased by you or a member of your household) | <input type="checkbox"/> Air conditioner |
| <input type="checkbox"/> Mattress or bed | <input type="checkbox"/> Bicycle |
| | <input type="checkbox"/> Motorcycle |
| | <input type="checkbox"/> Car or bakkie |

What is the highest grade you completed at school? _____ Grade completed

Have you completed any tertiary education (e.g. college, university)? Yes No

How many years of formal education did you receive (including primary, secondary, tertiary / university but excluding pre-school/creche)? _____ Years formal education

What is your current employment status?

- | | |
|---|----------------------------------|
| <input type="checkbox"/> Employed / self-employed – full time | <input type="checkbox"/> Retired |
| <input type="checkbox"/> Employed / self-employed – part time | <input type="checkbox"/> Student |
| <input type="checkbox"/> Unemployed | |

If you are employed:

How many **hours per week** do you work? _____ h/week

What time do you usually **start** work? _____ AM/PM

What time did you usually **end** work? _____ AM/PM

What best describes your **work schedule**?

- | | |
|---|---|
| <input type="checkbox"/> Day shift only | <input type="checkbox"/> Night shift only |
| <input type="checkbox"/> Rotating shifts with night shifts | <input type="checkbox"/> Irregular work hours |
| <input type="checkbox"/> Rotating shifts with no night shifts | |

Have you recently travelled abroad via plane? Yes No

If yes, What was your final destination? _____ (City, Country)

When did you arrive back in South Africa? _____ (Date home)

THE EPWORTH SLEEPINESS SCALE

INSTRUCTIONS

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently, try to work out how they would have affected you. Use the following scale to choose the most appropriate number for each situation:

0 = would never doze

1 = slight chance of dozing

2 = moderate chance of dozing

3 = high chance of dozing

Situation	Score (0 – 3)
Sitting and reading	
Watching television	
Sitting inactive in a public place (e.g. theatre or meeting)	
As a passenger in a car for an hour with out a break	
Lying down to rest in the afternoon when circumstances permit	
Sitting and talking to someone	
Sitting quietly after a lunch without alcohol	
In a car, while stopped for a few minutes in the traffic	
TOTAL score	

Appendix B – Sleep diary

ACTIVITY AND SLEEP DIARY

Participant ID code: _____

COMPLETE BEFORE BEDTIME								
Start date:	Example day Monday PM	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Today was a work/ school / off / sick day :	Work							
What time and for how long did you nap or doze today ?	17h30 20min							
Note any medication, supplements or drugs you took today : (e.g. over-the counter or prescription medications, recreational drugs, homeopathic formulations, vitamins)	Name: Parado Dose: 500mg Time: 13h35	Name: Dose: Time:	Name: Dose: Time:	Name: Dose: Time:	Name: Dose: Time:	Name: Dose: Time:	Name: Dose: Time:	Name: Dose: Time:
	Name: Multivitamin Dose: 1 caps Time: 07h00	Name: Dose: Time:	Name: Dose: Time:	Name: Dose: Time:	Name: Dose: Time:	Name: Dose: Time:	Name: Dose: Time:	Name: Dose: Time:
	Name: Dose: Time:	Name: Dose: Time:	Name: Dose: Time:	Name: Dose: Time:	Name: Dose: Time:	Name: Dose: Time:	Name: Dose: Time:	Name: Dose: Time:
Note any illness / symptoms you had today :	I had a cold and headache							
Note any physical activity or exercise session you did today (type, time, and intensity: easy, moderate, hard):	Walked the dog 06h30-07h00 (easy) Gym 18h30-19h30 (moderate)							

COMPLETE IN THE MORNING								
	Example day Tuesday AM	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Last night, I got into bed at :	10pm							
Last night I tried to go to sleep at (lights out, eyes closed):	10:20pm							
Last night, it took me minutes to fall asleep :	±10min							
I woke up for the last time this morning at (eyes open, lights on):	6am							
How satisfied were you with your sleep?	<input type="checkbox"/> Not at all <input type="checkbox"/> A little <input type="checkbox"/> Somewhat <input type="checkbox"/> Quite <input type="checkbox"/> Very	<input type="checkbox"/> Not at all <input type="checkbox"/> A little <input type="checkbox"/> Somewhat <input type="checkbox"/> Quite <input type="checkbox"/> Very	<input type="checkbox"/> Not at all <input type="checkbox"/> A little <input type="checkbox"/> Somewhat <input type="checkbox"/> Quite <input type="checkbox"/> Very	<input type="checkbox"/> Not at all <input type="checkbox"/> A little <input type="checkbox"/> Somewhat <input type="checkbox"/> Quite <input type="checkbox"/> Very	<input type="checkbox"/> Not at all <input type="checkbox"/> A little <input type="checkbox"/> Somewhat <input type="checkbox"/> Quite <input type="checkbox"/> Very	<input type="checkbox"/> Not at all <input type="checkbox"/> A little <input type="checkbox"/> Somewhat <input type="checkbox"/> Quite <input type="checkbox"/> Very	<input type="checkbox"/> Not at all <input type="checkbox"/> A little <input type="checkbox"/> Somewhat <input type="checkbox"/> Quite <input type="checkbox"/> Very	<input type="checkbox"/> Not at all <input type="checkbox"/> A little <input type="checkbox"/> Somewhat <input type="checkbox"/> Quite <input type="checkbox"/> Very
How refreshed/ rested do you feel this morning?	<input type="checkbox"/> Not at all <input type="checkbox"/> Slightly <input type="checkbox"/> Somewhat <input type="checkbox"/> Well- <input type="checkbox"/> Very well-	<input type="checkbox"/> Not at all <input type="checkbox"/> Slightly <input type="checkbox"/> Somewhat <input type="checkbox"/> Well- <input type="checkbox"/> Very well-	<input type="checkbox"/> Not at all <input type="checkbox"/> Slightly <input type="checkbox"/> Somewhat <input type="checkbox"/> Well- <input type="checkbox"/> Very well-	<input type="checkbox"/> Not at all <input type="checkbox"/> Slightly <input type="checkbox"/> Somewhat <input type="checkbox"/> Well- <input type="checkbox"/> Very well-	<input type="checkbox"/> Not at all <input type="checkbox"/> Slightly <input type="checkbox"/> Somewhat <input type="checkbox"/> Well- <input type="checkbox"/> Very well-	<input type="checkbox"/> Not at all <input type="checkbox"/> Slightly <input type="checkbox"/> Somewhat <input type="checkbox"/> Well- <input type="checkbox"/> Very well-	<input type="checkbox"/> Not at all <input type="checkbox"/> Slightly <input type="checkbox"/> Somewhat <input type="checkbox"/> Well- <input type="checkbox"/> Very well-	<input type="checkbox"/> Not at all <input type="checkbox"/> Slightly <input type="checkbox"/> Somewhat <input type="checkbox"/> Well- <input type="checkbox"/> Very well-
Was this a typical night ? (Yes or No)	Yes							

FAQs and GENERAL INSTRUCTIONS

What is this Diary for? This diary is designed to gather information about your daily sleep and activity patterns and possible factors which might affect your sleep.

How often and when do I fill out the Diary? Please complete your diary every day for 7 days. The "Complete before bedtime" section should be completed before you go to bed at night. The "Complete in the morning" section should be completed within one hour of getting out of bed in the morning.

What should I do if I miss a day? If you forget to fill in the Diary, leave the diary blank for that day.

What if something unusual affects my sleep or how I feel in the daytime? If you experience an unusual event (such as an illness, or an emergency) on a given day, you may wish to make brief notes in the "Additional Comments" section below.

Use the guide below to clarify what is being asked for each item of the Diary.

- 1. Today was a work/ school / off / sick day:** Please note whether or not you worked or went to school/college/university today. Off-days may include weekend days, public holidays, sick days.
- 2. What time and for how long did you nap or doze?** A nap is a time you decided to sleep during the day, whether in bed or not in bed. "Dozing" is a time you may have nodded off for a few minutes, without meaning to, such as while watching TV. Note all the times you napped or dozed from when you first got out of bed in the morning until you got into bed again at night. If you did not nap, write "N/A" (not applicable).
- 3. Note any medication, supplements or drugs you took today** (e.g. over-the counter or prescription medications, recreational drugs, homeopathic formulations, vitamins): Record any over-the counter or prescription medications, recreational drugs, homeopathic formulations or vitamins/minerals that you used – whether usual or once-off. Record the name, dose and time you took each product today.
- 4. Note any illness / symptoms you had today:** Please note down any illness and / or symptoms you experienced during this day. If you did not experience any illness/symptoms, write "N/A".
- 5. Note any exercise session you did today** (type, time): Record the type of exercise session you did today (e.g. walk, hike, yoga, gym, run, swim, tennis etc) as well as time-of-day you started and ended the session. If you did not exercise, write "N/A".
- 6. Last night, I got into bed at:** This is the time you physically get into bed, perhaps to read, but are not yet trying to sleep.
- 7. Last night I tried to go to sleep at** (lights out, eyes closed): Record the time that you began "trying" to fall asleep (i.e. lights out and eyes closed).
- 8. Last night, it took me minutes to fall asleep:** Beginning at the time you began trying to fall asleep, estimate how long it took you to fall asleep.
- 9. I woke up for the last time this morning at** (eyes open, lights on): Record the time you woke up in the morning to begin your day (i.e. lights on and/or eyes open, you are no longer trying to sleep).
- 10. How satisfied were you with your sleep?** Sleep "satisfaction" is your sense of whether your sleep was good or poor.
- 11. How refreshed / rested did you feel when you woke up for the day?** This refers to how you felt after you were done sleeping for the night, during the first hour after you woke up.
- 12. Was this a typical night** (Yes or No): Note whether this night was representative of what you usually experience.

ADDITIONAL COMMENTS (Please feel free to make additional notes about the week here):