UNIVERSITY OF BIRMINGHAM

School of Sport, Exercise and Rehabilitation Science

MSc By Research Thesis: Emily Senior

1419068

Supervisors: Dr. George Balanos, Dr. Sam Lucas

"Physical Activity to Reduce Obstructive Sleep Apnoea: A 12-Week Intervention."

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1. Abstract

It has previously been shown that exercise can reduce the severity of obstructive sleep apnoea (OSA). This effect has been shown to occur both with, and independent of, a reduction in weight or change in body mass index (BMI). A combination of the increased risk of cardiovascular disease caused by OSA and generally low adherence to the current treatment by continuous positive airway pressure (CPAP) calls for further research into the use of structured exercise or daily physical activity as an alternative treatment. This study tested a 12-week gradually increasing physical activity intervention to reduce severity of OSA in adults independent of a change in weight. Data from 13 participants (6 females, 7 males) were collected at baseline and after a 12-week physical activity intervention. The intervention involved 3 lots of 10 minutes of physical activity at a rate of perceived exertion (RPE) of 9 in week 1, which steadily increased to 5 lots of 30 minutes of physical activity at an RPE of 13 in week 12. From pre- to post-intervention there was a significant increase in physical activity ($p<0.01$), and a significant decrease in the severity of OSA ($p<0.01$). No significant changes in BMI ($p=0.97$) were recorded. A moderate to low but non-significant correlation between the change in OSA severity pre to post intervention and the percentage increase in physical activity over the intervention ($p=0.466$) was found along with a significant interaction between change in severity of OSA and change in body fat percentage ($p<0.01$). These results suggest that physical activity can reduce the severity of OSA, with a possible dose dependent relationship suggesting that physical activity cannot be ruled out as a cost-effective alternative management tool for moderate to severe OSA. The interaction of change in body fat percentage included in the analysis could lead to further research into the effect of fatty deposits in the upper airway muscles, and strength and activity of these muscles as a possible mechanism for the reduction that is seen.

Keywords: Physical Activity; Obstructive sleep apnoea; sleep disorders; Exercise

Abbreviations

AHI	Apnoea-Hypopnoea Index
ANOVA	Analysis of Variance
BIA	Bioelectrical Impedance Analysis
BMI	Body Mass Index
CPAP	Continuous Positive Airway Pressure
CRP	C-Reactive Protein
EEG	Electroencephalogram
EMG	Electromyography
ESS	Epworth Sleepiness Scale
IH	Intermittent Hypoxia
IL-6	Inter Leukin 6
IPAQ	International Physical Activity Questionnaire
MSLT	Multiple Sleep Latency Test
MVPA	Moderate to Vigorous Physical Activity
OSA	Obstructive Sleep Apnoea
PA	Physical Activity
$PaCO_2$	Partial Pressure of Carbon Dioxide
PaO_2	Partial Pressure of Oxygen
RDI	Respiratory Disturbance Index
RPE	Rating of Perceived Exertion
SaO_2	Blood Oxygen Saturation
T2D	Type 2 Diabetes
TNF-α	Tumour Necrosis Factor Alpha
UAS	Upper Airway Stimulation

2. Introduction

2.1 Obstructive sleep apnoea

Obstructive sleep apnoea (OSA) is a breathing disorder in which the upper airways repeatedly collapse during sleep causing restricted airflow (hypopnoea) or cessation of breathing (apnoea). Moderate to severe OSA is diagnosed in 9% of middle aged men and 4% of women of the same age (Al Lawati, Patel and Ayas, 2009), however, it is likely that up to 85% of sufferers remain undiagnosed (Rejon-Parrilla, Garau and Sussex, 2014). OSA risk factors include obesity, sex, craniofacial differences, alcohol consumption and smoking (Al Lawati, Patel and Ayas, 2009), but the exact cause is still uncertain as none of these factors can fully predict OSA risk or severity. The severity of OSA is described by the apnoea-hypopnoea index (AHI), which represents the number of apnoea's and hypopnoea's per hour of sleep. An apnoea is defined as the cessation of airflow for at least 10 seconds and hypopnoea is defined as a 30% reduction in airflow for 10 seconds with a 4% reduction in blood oxygen saturation, or a 50% reduction in airflow for 10 seconds with a 3% reduction in blood oxygen saturation (Al Lawati, Patel and Ayas, 2009). The severity of sleep apnoea is classified in categories of mild, moderate, and severe corresponding to an AHI of 5-15, 15-30 and >30 respectively (Flemons W.W., 1999). AHI is tested using polysomnography and other home testing tools like the ResMed ApneaLink. Testing for OSA includes, at minimum, the monitoring of air flow, oxygen saturation in the blood, and effort of breathing. These factors determine if and when apnoea and hypopnoea events occur and how often. Polysomnography is the gold standard as it uses electroencephalogram (EEG) to determine sleep stages.

2.2 Implications of obstructive sleep apnoea

OSA is problematic not only because it causes excess daytime sleepiness and reduces quality of life (Al Lawati, Patel and Ayas, 2009), but it also causes a diminished probability of long-term survival. Floras (2014), showed that 1.06 in every 100 people with OSA die as a result of a cardiovascular event which is considerably higher than the 0.3 in every 100 healthy adults. Additionally, 30% of people with hypertension are also diagnosed with OSA (Al Lawati, Patel and Ayas, 2009) and it has been shown that severity of hypertension and AHI are positively associated (Kent, Ryan and McNicholas, 2011). Zhang and Si (2012), furthered this by showing that normalisation of blood pressure can reduce OSA in rats suggesting that not only is hypertension an adverse consequence, but it could also be a cause of OSA. Similarly, 71% of type-2 diabetes (T2D) patients are also diagnosed with OSA (Pamidi and

Tasali, 2012). However, it is uncertain whether OSA affects glucose tolerance over time or vice versa. OSA and other sleep disordered breathing conditions have been shown to increase the relative odds of being diagnosed with heart failure, stroke and coronary heart disease (SHAHAR *et al.*, 2001), additionally, studies have shown that patients with an AHI of >20 have a greater mortality rate from these cardiovascular diseases (He *et al.*, 1988) and stroke (Arzt *et al.*, 2005).

The strong relationship between cardiovascular events and OSA is of great clinical and public health importance and therefore it is valuable to study the mechanisms that lead to such problems. Figure 1 demonstrates the cyclical events of an apnoea and highlights the different physiological stressors that may result in harmful implications. These include significant changes in intrathoracic pressure, intermittent whole body hypoxia, reoxygenation and increased arousal of the sympathetic nervous system (Golbin, Somers and Caples, 2008).

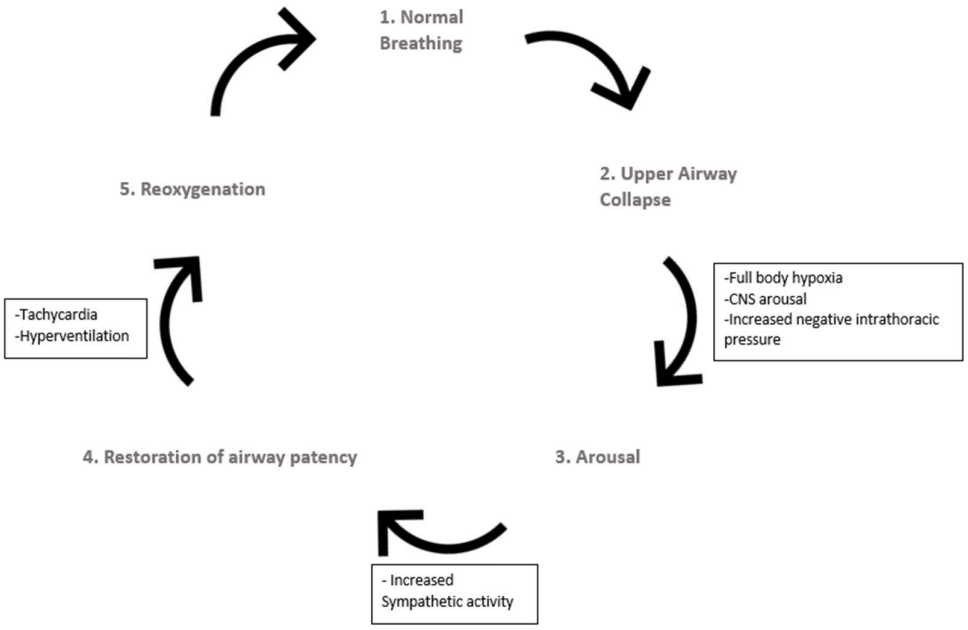

Figure 1. *Cyclical physiological events of an apnoea.*

Intrathoracic Pressure

Normal breathing occurs due to the contraction of the respiratory muscles, causing expansion of the thorax. The difference in pressure between the environment and the alveoli, caused by

this expansion, leads to a negative pressure in the upper airway and air is drawn into the lungs (Edwards and White, 2011). In patients with OSA, the upper airway is narrowed therefore leading to greater airway resistance and negative pressure and increasing vulnerability to collapse (Schwab *et al.*, 2003). Further contributing to the risk of airway collapse, OSA patients have been shown to have reduced activity of the genioglossus muscle (Edwards and White, 2011; Mezzanotte, Tangel and White, 1992), which is an upper airway dilator. During an airway collapse, the patient makes repeated attempts to breath at increasing efforts against an occluded airway which causes a greater negative intrathoracic pressure (Sforza, Krieger and Petiau, 1998). In rats, repeated inspiratory occlusions have been shown to cause acute cardiac dysfunction (Simpson, Brunt and Iscoe, 2008). Similarly, in humans, negative intrathoracic pressure leads to decreased stroke volume, increased venous return (Orban *et al.*, 2008) and increased pulmonary artery pressure (Marrone *et al.*, 1994). Reduced stroke volume affects the preload and afterload of the heart (Bonsignore *et al.*, 1994) which can lead to impediment of left ventricular filling. These effects combined, lead to congestion of blood in the pulmonary circulation and reduction in oxygenation of major organs and tissues as less blood is pumped from the heart.

Full body Hypoxia

OSA patients are frequently exposed to whole body hypoxia as the partial pressure of oxygen in the alveoli gradually falls during an apnoea and causes the blood oxygen saturation (SaO_2) to fall as well. The reopening of the airway, caused by a transient partial arousal to restore airway patency, causes the SaO_2 to be rapidly restored following each apnoea, with the fluctuation of SaO_2 known as intermittent hypoxia (IH). It is likely that IH is a cause of further harmful cardiovascular and myocardial complications (Floras, 2014). It is also suggested that IH and fragmented sleep may be the cause of derangement in glucose metabolism in T2D via excess inflammation (Pamidi and Tasali, 2012) and that IH stimulates chemoreceptor activity leading to vasoconstriction and hypertension (Foster, Poulin and Hanly, 2007). In order to determine the impact that IH has on cardiovascular factors, it needs to be studied in the absence of mechanical OSA stimuli, such as occluded inspiratory effort. Both IH and inspiratory efforts have been shown to induce systemic inflammation, but IH alone also induces endothelial dysfunction (Nacher *et al.*, 2009). Four weeks of IH in rats elicited an increase in pulmonary hypertension (Fagan, 2001) while other animal studies also

show that chronic IH, similar to that seen in OSA, increases sympathetic activation (Sica *et al.*, 2000), atherosclerosis (Savransky *et al.*, 2007) and myocardial dysfunction (Williams, Chen and Scharf, 2010) in the absence of inspiratory effort. IH may cause hypertension and other cardiovascular issues via increases in circulatory inflammatory proteins and lead to the release of oxygen derived free radicals which negatively impacts endothelial function (Kent, Ryan and McNicholas, 2011; Sawatari *et al.*, 2016; Lavie, 2012; El Solh *et al.*, 2006; Lévy *et al.*, 2008). Oxidative stress occurs when there are too many free radicals in the blood or not enough antioxidants to buffer them and both can inhibit normal cellular function. OSA patients have been shown to have elevated markers of oxidative stress and reduced antioxidant capabilities (Mancuso *et al.*, 2012; Jelic *et al.*, 2010; Pialoux *et al.*, 2009).

Reoxygenation

Reoxygenation of tissues occurs after all IH events in OSA patients. Reoxygenation injury also known as reperfusion injury or ischemia-reperfusion injury, occurs when tissues have been starved of oxygen and are re-perfused with oxygen rich blood. Reoxygenated mitochondria produce excess superoxide, reactive oxygen species and other by-products which react with protein and lipid membranes and affect cellular function (Li and Jackson, 2002; Samarasinghe, Tapner and Farrell, 2003). Superoxide generation during OSA is likely to be linked to the development of cardiovascular disorders (SCHULZ *et al.*, 2000; Lavie, 2003).

Inflammatory pathways

Activation of inflammatory pathways like tumour necrosis factor-α (TNF-α) (Ryan, Taylor and McNicholas, 2005) or C-Reactive Protein (CRP) (Shamsuzzaman *et al.*, 2002) in OSA are also suggested to be the mechanisms of cardiovascular disease in this population. TNF-α has been shown to be elevated in obese patients as well as those with OSA (Bhushan *et al.*, 2009; Popko *et al.*, 2008) and both IH and inspiratory efforts have been shown to play a role in the induction of systematic inflammation (Nacher *et al.*, 2009). This affects the cardiovascular system as TNF-α plays a role in initiation, progression, and severity of coronary artery disease (Lona *et al.*, 2013). CRP is also linked to cardiovascular risk factors (Kablak-Ziembicka *et al.*, 2011) however, although obesity and IH are variables that have

been shown to increase CRP (Kapsimalis, Varouchakis and Gourgoulianis, 2005), another study found that there was no independent correlation between CRP and OSA (Sharma *et al.*, 2008) so it is unlikely to be the main mechanism relating OSA to cardiovascular disease.

Arousal of the sympathetic nervous system

During an apnoea there is an increase in sympathetic nerve activity which is exaggerated by the hypoxemic environment (Smith *et al.*, 1996; Somers, Dyken and Skinner, 1993). Cycles of decreased oxygen (hypoxia) and increased carbon dioxide (hypercapnia) causing increased sympathetic nerve activity can cause peripheral vasoconstriction and increased heart rate (Bradley and Floras, 2003). However, an exaggerated chemoreflex in patients with OSA may be the cause of more acute increases in peripheral vasoconstriction and arterial blood pressure (Golbin, Somers and Caples, 2008). In order to restore the patency of the upper airways and oxygen circulation, it is likely that an arousal occurs in response to increased chemoreceptor drive stimulated by the increase $PaCO_2$ and decreased PaO_2 (Sforza, Krieger and Petiau, 1998). However, it may also be due to the increased ventilatory effort during an apnoea (Gleeson, Zwillich and White, 1990). This arousal event causes further elevation of sympathetic nerve activity leading to transient tachycardia and hyperventilation to reoxygenate the body. The increase in sympathetic nerve activity also contributes to an increased peripheral vascular resistance (Morgan *et al.*, 1996) which has negative cardiovascular implications. These sympathoexcitatory cardiovascular effects of arousal are relatively long lasting and could accumulate after repetitive arousals leading to further implications (Blasi *et al.*, 2003).

Level of physical activity

While low levels of physical activity (PA) have been shown to be associated with OSA (Simpson *et al.*, 2015; Verwimp, Ameye and Bruyneel, 2013), a reduction in physical activity is also an implication of the disease. Symptoms like daytime sleepiness, increased anxiety levels and fatigue may cause this low level of physical activity in OSA patients (Caliskan *et al.*, 2019), however, the reverse may also be true, and the low levels of physical activity could be the cause of the symptoms. What is known is that cardiovascular disease, T2D and increased chance of stroke are directly associated with lack of physical activity and it is

therefore difficult to separate the impact of OSA from the impact of lack of physical activity. This has been a major factor inspiring the current research and previous studies looking at physical activity, exercise and OSA.

2.3 Obstructive sleep apnoea and obesity

Like many diseases, OSA is positively correlated with obesity. There are two ways in which obesity can affect OSA: (i) abdominal mechanisms and (ii) neck related mechanisms.
(i) Obesity causes OSA due to increased abdominal pressure and reduced movement of the ribcage and diaphragm (Araghi *et al.*, 2013), which is most common in central obesity (Tan *et al.*, 2015). Al Lawati, Patel and Ayas (2009), agree with this and suggests that obesity reduces lung volume and alters airway function. However, they also argue that OSA alters the activity of satiety hormones leptin and ghrelin which suggests that OSA could be a cause of obesity rather than the other way around. The authors do not commit to this suggestion but rather put forward the concept of a vicious cycle with both obesity and OSA impacting on each other. Nevertheless, reviews of recent studies have shown that intensive lifestyle interventions to reduce weight are successful in reducing both BMI and AHI in patients with diagnosed OSA (Araghi *et al.*, 2013; Thomasouli *et al.*, 2013).
(ii) Neck circumference has been shown to have a stronger correlation with AHI than the correlation seen between AHI and BMI (Tom *et al.*, 2018). A recent study on Asian patients supports this finding having shown that neck circumference can predict the presence and severity of OSA (박강민 *et al.*, 2015). Fatty tissue deposits in and around the upper airway causing the increased neck circumference can lead to a decreased upper airway lumen size (Corgosinho *et al.*, 2020). An anatomically narrow upper airway is a major risk factor for OSA (Schwab *et al.*, 2003) as it augments negative pressure during inspiration, and it increases the likelihood of upper airway collapse.

Although more common in overweight and obese patients, OSA is still, albeit occasionally, seen in patients of a normal weight. In a study of 475 patients, just 7.6% of the normal weight patients had OSA compared to the 56.4% of obese patients (Quintas *et al.*, 2013). Interestingly, normal weight patients with OSA were more likely to be younger women which is contradictory to the previously suggested risk factors for OSA. Normal weight OSA patients have more apnoeas, whereas overweight patients have more hypopnoeas and a lower minimum SaO_2 (Dreher, Patscheider and Braun, 2012). Additionally, Carrera *et al.,* (2004),

suggested that non-obese OSA patients had greater fatigability of the genioglossus compared to healthy controls, this difference was not present in obese OSA patients. The reason behind these differences is currently unknown, but Brodovskaya *et al.* (2019) suggest that it may be related to the increased risk of visceral fat obesity that is seen in normal weight OSA patients. It is suggested that upper airway contractile force is decreased by fatty deposits in muscle (Corgosinho *et al.*, 2020). Visceral fat could therefore affect the contractile strength of the diaphragm and other respiratory muscles in normal weight OSA patients. However, Brodovskaya *et al.* (2019) also acknowledge the likelihood that an increase in visceral fat could be caused by OSA and other pathophysiological mechanisms that accompany it, for example intermittent hypoxia, oxidative stress and other inflammatory pathways that affect adipogenesis. Therefore, the cause of OSA in normal weight patients remains unknown.

2.4 Treatment of obstructive sleep apnoea.

The most common treatment of OSA is by use of a continuous positive airway pressure (CPAP) machine during sleep. CPAP prevents the collapse of the airways by applying continuous air pressure via a mask, therefore reducing snoring, and preventing intermittent hypoxia that is caused by apnoeas and hypopnoeas. CPAP is highly recommended for patients that have excessive day time sleepiness as a symptom as it can improve sleep quality (Gottlieb and Punjabi, 2020). Reviews of the effectiveness of CPAP have shown that it is able to reduce inflammatory markers in the blood of OSA sufferers (Kent, Ryan and McNicholas, 2011) and attenuate signs of oxidative stress (Lavie, 2012). However, not all research has found comparable results when studying the effects of CPAP. In other reviews, Bradley and Floras (2009) suggests that CPAP is effective at reducing blood pressure in patients with OSA but has no effect on glycaemic control, whereas Pamidi and Tasali (2012) suggest that the use CPAP is associated with a significant reduction in diabetes prevalence in OSA patients. The results of these studies may be affected by adherence to the use of a CPAP: Yetkin, Kunter and Gunen (2008) studied 71 patients with a mean AHI of 43.5, all patients had excessive daytime sleepiness measured by the Epworth sleepiness scale (ESS) and had nocturnal snoring; despite the well-established benefits of CPAP, this study found that CPAP compliance had a positive correlation with AHI meaning that those with less severe OSA were less likely to use their CPAP regularly. This finding may be due to the less severe OSA patients having less severe daytime symptoms and therefore a lesser sense of satisfaction with the treatment. This is highlighted by the correlation that was also found

between CPAP coherence and ESS in the same study. However, Yetkin, Kunter and Gunen (2008) established CPAP compliance levels via self-report which may be unreliable as participants may feel the need to report higher compliance than is actually achieved. Education can increase CPAP use by up to 25% (Cvengros *et al.*, 2016), and eHealth interventions have also been shown to improve adherence (Aardoom *et al.*, 2020), for example the sleepwell24 smartphone app (Petrov *et al.,* 2020). Without these interventions in place, low adherence diminishes the effectiveness of the CPAP treatment (Sawyer *et al.*, 2011). Furthermore, it has been shown that despite the benefits of CPAP (reducing signs of oxidative stress, reducing inflammatory markers in the blood, reduced snoring, and daytime sleepiness (McEvoy *et al.,* 2016)) once CPAP ceases, benefits are quickly reversed (Floras, 2014). This suggests that CPAP is solely a treatment for the symptoms of OSA and not a treatment for the disease itself. A systematic review by Thomasouli *et al.*, (2013) found that studies including a lifestyle change were more effective at managing OSA compared to CPAP use. This is supported by an 18 month follow up study showing that 37.5% of participants in an experimental group, treated with physical activity, healthy eating and CPAP, had an improvement in OSA, compared to the 7% that improved when treated only with CPAP (Sporndly-Nees *et al.*, 2020). This research informs our current research into physical activity as a way to reduce OSA without the use of CPAP, however the current research will differ as it will focus on physical activity alone, not a combination of PA and eating behaviour. McEvoy *et al.* (2016), further supported this as findings show that treatment with CPAP does not prevent cardiovascular events in patients with moderate to severe OSA so providing us with an additional argument for using physical activity to treat OSA as regular physical activity, can decrease the incidence of cardiovascular disease and even light intensity PA is inversely associated with all-cause mortality (Winzer, Woitek and Link., 2018).

Other treatments like oral pressure devices, mandibular advancement devices, and positional therapies have been trialled as treatments. Oral appliances can be used effectively to compliment positive pressure treatment and can be efficient in some patients when CPAP is not tolerated with an average reduction of an AHI of 10.4 (Skalna *et al.*, 2019). In particular, Maxillomandibular advancement has been shown to be an effective long-term treatment that is equivalent to CPAP for decreasing AHI and subjective sleepiness (Boyd *et al.*, 2015). However, the Skalna *et al.*, 2019 research was done by a company that makes such appliances so may have some bias, it also includes participants with an AHI below 5 and with

a diagnosis of primary snoring. These participants should be removed from analysis to better represent the target population. Sleep position therapy can also improve sleepiness and sleep quality in patients with position-dependent OSA (van Maanen and de Vries, 2014), a type of OSA that is exaggerated when the patient is in a supine position. However, improvements in AHI were not reported in this research and not all OSA is position dependent so therefore further treatment needs to be explored for all types of OSA. Surgical interventions are another option for treatment of OSA. Barbed repositioning pharyngoplasty appears to be a promising treatment, especially in patients with severe OSA (Vicini *et al.*, 2019). Similarly, 3- and 6-months post robotic base resection or uvulopharyngoplasty surgery there is a reported effectiveness matching that of CPAP treatment (Kersin *et al.*, 2019). However, the patients in this study also reported significant weight loss which may be the reason for the improvements. On the other hand, as has been suggested earlier, the improvement in OSA may have contributed to weight loss.

Rousseau *et al.* (2016) report that transcranial magnetic stimulation of the genioglossus does not increase airflow, however, direct upper airway muscle stimulation (UAS) is shown as an effective treatment in OSA patients with a BMI below 40 (Weaver *et al.*, 2014). This suggests that direct stimulation may work as a treatment for OSA, but indirect stimulation is not effective. It is suggested that UAS would be a cost-effective way to treat OSA relative to costs of cardiovascular diseases that could occur if not treated (Pietzsch *et al.*, 2015). UAS is particularly relevant to the topic of this current paper as activation and stimulation of the upper airway muscles increase with physical activity. Therefore, the mechanisms of UAS could relate to the affects that align with the hypothesis of this paper.

2.5 Obstructive sleep apnoea and Exercise.

Even with an abundance of available research into OSA, the causal mechanisms of the disease are still unknown and without this information it is challenging to treat the problem directly. Evidence is building for the use of exercise as a treatment for OSA. A large number of OSA patients experience exercise limitations when tested by the 6-minute walk distance test (Vitacca *et al.*, 2020). Equally people classified as more active by the international physical activity questionnaire were found to have a lower AHI (Monico-Neto *et al.*, 2018) whilst, people who are less active are more likely to have a higher AHI (Verwimp, Ameye and Bruyneel, 2013; Simpson *et al.*, 2015; Hall, Singh and Mukherjee, 2020). In addition,

Igelstrom (2015) supported this by showing that people with higher daily sedentary time have a higher risk of OSA. Kline *et al.* (2014) analysed the inverse relationship between physical activity and OSA risk and found it to be dose dependent, however the relationship is based on self-reported physical activity and risk of OSA determined by a screening questionnaire. This relationship should be investigated using objective measures of physical activity and diagnostic measures for OSA for more reliable results. The current study will begin to explore this relationship with these objective measures. Combined, these articles could suggest that exercise or physical activity could be used to treat the disease itself, rather than just the symptoms. For the purpose of this study, an intervention is classed as exercise when it includes supervised or structured activities that the participant must adhere to, whereas physical activity interventions will be referred to if interventions use unsupervised and unstructured activity to increase in daily movement. There are no consistent exercise programmes used across studies to test the effect of exercise or physical activity on sleep apnoea; but, results demonstrating the ability of exercise to reduce OSA severity seem to be consistent. Giebelhaus *et al.* (2000) used alternating supervised aerobic and stamina exercise training for six months with a group of 11 participants with moderate to severe sleep apnoea and found that their Respiratory disturbance Index (RDI) was reduced significantly from a mean of 32.8 events per hour to 23.6 events per hour; Kline (2011) studied 43 overweight or obese participants with moderate to severe OSA for 12 weeks and the intervention consisted of 150 minutes of moderate aerobic exercise per week and two supervised resistance training sessions, their results showed a significantly reduced AHI from a mean of 32.2 events per hour to a mean of 24.6 events per hour; Redolfi *et al.* (2015) tested 8 non-severely obese participants with moderate to severe OSA in one week, providing two 45min moderate speed walking sessions per day, they found that the mean AHI of 58 events per hour prior to the intervention was significantly reduced to 40.6 events per hour; all of these exercise training methods produced results showing a reduction in AHI, but differ from the current study as the exercise was supervised and structured whereas the current study will use unsupervised physical activity in which only advice on frequency, duration and intensity is given but mode of exercise is the participants choice. The importance of a tailored physical activity and eating behaviour intervention as an adjunct to CPAP to treat OSA has been emphasised due to its longer-term benefits, a study of 60 participants in an 18 month follow up study found that 36.7% of participants in the CPAP plus behavioural management group had improvement in OSA category at 18 months follow-up, whereas just 6.7% of those treated with just CPAP had an improvement (Sporndly-Nees *et al.,* 2020). Additionally, a recent

longitudinal study showed that a supervised exercise programme can lead to a 61% reduction in the incidence of OSA and a significant reduction in AHI at a 4-year follow up evaluation of these patients (Tuomilehto, 2013), however this study only included participants with mild OSA which is not representative of the community OSA population. Supervised and unsupervised exercise have both been shown to reduce AHI, however, supervised exercise has been shown to improve cardiovascular disease, fatigue, and glucose tolerance better than unsupervised exercise (Iftikhar, Kline and Youngstedt, 2014). This could be due to adherence to the exercise programme. For example, Picorelli *et al.* (2014) reviewed studies of high-risk populations (>65 years old) and showed that adherence to exercise is generally better in supervised programs. This could suggest that the improvement in OSA severity is a function of how much exercise the participants are doing and questions the feasibility of unsupervised interventions. However, unsupervised home-based physical activity programs have been shown to be effective when the participants are part of an organised group (Jurkiewicz, Marzolini and Oh, 2011). This effectiveness may be linked to goal setting and positive reinforcement as this has been shown to improve adherence (Conraads *et al.*, 2012). The current study will aim to implement things like goal setting and positive reinforcement to uphold adherence. While the majority of research displays the effectiveness of exercise in treating OSA, one study found that individualised exercise training did not decrease AHI when compared to a control group (Bughin *et al.,* 2020). However, the researchers still suggested that individualised exercise programs should be considered to manage OSA as daytime sleepiness, measured objectively by the multiple sleep latency test (MSLT), did find improved daytime sleepiness, additionally in the intervention group AHI was improved when looking at REM sleep alone. Moreover, research by Vincent *et al.* (2002) suggests that physical activity only reduces central sleep apnoea and not OSA. However, the participants in that study were all heart failure patients, so it is difficult to generalise these findings within a wider population. Further research is required to determine the minimum and optimal amounts of physical activity needed to reduce sleep apnoea and establish if physical activity rather than exercise can be used as an effective alternative treatment.

As previously discussed, obesity is a major risk factor for OSA. Therefore, it is likely that weight loss as a result of exercise and/or diet intervention could be the mechanism for the reduction in OSA. A 2013 review found that although exercise was able to reduce AHI, the reduction was dependent on a reduction in weight (Araghi *et al.*, 2013). Dobrosielski *et al. (*2015), showed that a 12-week weight loss programme incorporating a change in diet and

exercise can be used to reduce AHI in obese adults with OSA that are over the age of 60. Similarly, weight loss due to diet alone has also shown similar reductions in AHI (Plourde and Kline, 2013; Tuomilehto, 2013). However, Plourde and Kline 2013 used a single participant case study which makes the results hard to generalise. The previously mentioned long-term follow-up study by Tuomilehto (2013) showed that the reduction in the incidence of OSA was not independent of weight loss, in fact weight loss was a focus of the initial exercise intervention that the participants took part in. Furthermore, A nine-month community-based exercise programme saw 58% of participants with a moderate OSA reduce their AHI to below 15 (Berger *et al.*, 2018). Researchers found that this exercise effect was greater in obese participants suggesting a positive linear relationship between weight loss and AHI reduction. Berger *et al.* (2018), also suggested a potential correlation with pharyngeal fat in causing the reduction of AHI which aligns with the aforementioned research on the effect of obesity and the collapsibility of the upper airways (Tom *et al.*, 2018). Nonetheless, Anandam *et al.* (2013), suggested that although weight loss can effectively reduce AHI, it is not a curative therapy as it cannot relieve all respiratory events and prevent all apnoeas and hypopnoeas. This is supported by Mendelson *et al.* (2018) as they argue that CPAP can reduce symptoms of OSA despite an increase in body weight suggesting that there are other mechanisms vital to OSA.

More recent studies have found that exercise may effectively reduce OSA by as much as 28%, even in the absence of weight loss or change in BMI (Mendelson *et al.*, 2018). Researchers have found AHI reductions independent of BMI change in a variety of exercise programmes of varying lengths including supervised and unsupervised exercise (Aiello *et al.*, 2016; Giebelhaus *et al.*, 2000; Kline, 2011; Redolfi *et al.*, 2015). Furthermore, a review of previous studies found that more active people, measured by a range of questionnaires and activity sensors, were found to have a lower AHI independent of body weight (Van Offenwert *et al.*, 2019). Another review found that exercise interventions, lasting between 12 and 24 weeks, can lead to a reduction in AHI equivalent to that seen with a 10% reduction in body weight (Iftikhar, Kline and Youngstedt, 2014). Another study found that supervised exercise can not only reduce AHI but also improve sleep quality despite no significant weight loss (Kline, 2011). During an exercise program, although weight may not change, adipose tissue could be redistributed to muscle suggesting that AHI changes might be linked to changes in body composition. Considering the inability of the BMI scale to differentiate between adipose and muscle tissues, the current study will utilise the more comprehensive

anthropometric measure of bioelectrical impedance to measure the body fat percentage of participants before and after an exercise programme.

Exercise has been shown to increase the recruitment of upper airway muscles in rats (Vincent *et al.*, 2002). Similarly, in humans, exercise has been shown to increase skeletal muscle tone, including the pharyngeal muscles, and increase ventilatory drive. This is potentially due to engagement of pharyngeal and glossal muscles during training (Giebelhaus *et al.*, 2000), suggesting that exercise may specifically improve muscle tone of the upper airways and therefore reduce their collapsibility during sleep. This was supported by Sands *et al.* (2014) whose comparison of overweight patients with and without OSA showed that although both groups had a similarly compromised structure of the upper airway, those without OSA were less prone to collapse than those with OSA as they had greater upper airway muscle responsiveness which was measured by EMG during sleep at different levels of CPAP pressure. Although further research is required, research does support the possibility that weight loss is not a necessary component of OSA treatment and other mechanisms relating to muscle tone and the upper airway may be more relevant.

2.6 Management of obstructive sleep apnoea by physical activity or exercise

The evidence tells us that physical activity could be effective in the management and treatment of OSA. For example, a review of 8 relevant clinical trials including 228 participants concluded that exercise improves subjective parameters like day time sleepiness by a mean of 3.7 on the Epworth sleepiness scale as well as OSA severity by a mean AHI reduction of 11.4 (Lins *et al.,* 2020) and in healthy people exercise increases the drive to breathe (Giebelhaus *et al.*, 2000) which could reduce the collapsibility of the airways during sleep. Similarly, this reduction in collapsibility could be due to the recruitment of upper respiratory muscles during exercise which may persist in the periods after exercise (Vincent *et al.*, 2002), however this study was done in rats so further research is necessary in humans. Additionally, it has been shown that a six-month cardiac rehabilitation programme which improved exercise capacity can improve OSA in heart failure patients (Yamamoto, 2007) further supporting the use of exercise or physical activity to manage OSA in this specific group of patients. Alternatively, weight loss may be the cause of the reduction in AHI due to the reduction of pressure on the upper airways making them less collapsible. This is supported by Redolfi *et al.* (2015) demonstrating that increasing movement, using a 1 week intervention including 2 lots of 45 minute sessions of moderate walking per day, reduces

fluid shift from the legs to the neck which reduces nocturnal pressure on the airways, measured by change in nocturnal pharyngeal air volume, and subsequently significantly reduces AHI. Although evidence generally remains inconclusive, physical activity can be used for general health improvement and therefore would be a beneficial management tool for OSA.

Further consideration should be given to the type of physical activity that would be most beneficial for OSA patients. Moderate to vigorous physical activity (MVPA) makes up less than 5% of most people's day (Chaput *et al.*, 2014) suggesting that it could be more important to consider lower level exercise, namely physical activity, and sedentary time as potential predictors and treatments for sleep apnoea. This is supported by Igelström *et al.* (2018), who showed that low physical activity levels and high sedentary time are related to OSA risk. Walking and activities of daily living have been shown to be easier to work into daily routine than structured exercise and therefore are likely to be more sustainable as a treatment (Chaput et al., 2014). Moreover, it is important to consider the accuracy of how physical activity and intensity is measured in research and if it was to be used as treatment to ensure participants and patients are adhering to interventions and treatment plans. International physical activity questionnaires (IPAQ) are known and accepted as a means of recording repeatable and valid data having been used in 12 different countries among adults from 18 to 65 years old (Craig et al., 2003) and Borg's Rate of Perceived Exertion Scale (RPE) is a practical tool for monitoring intensity of physical activity which is strongly correlated with heart rate and blood lactate levels (Scherr et al., 2013). These measures will be used in the current research.

2.7 Hypothesis

The aims of the current study are to see if an increase in daily physical activity can improve the severity of OSA, and to see if this change is related to weight loss or not. The hypothesis is that participants who are able to gradually increase their daily physical activity over a 12-week intervention period will have reduction in the severity of the OSA that they experience.

3. Methodology

3.1. Participants

Using posters, leaflets and social media, recruitment targeted volunteers who reported snoring and/or daytime sleepiness. Recruitment responders were offered a home test to assess

whether they were unknowingly OSA sufferers. Participants were included in the study if they had an AHI of 15 (See Appendix A) or above after two nights of testing, if they had not been advised to avoid exercise for any reason by their doctor and if they were willing to participate in a 12-week physical activity programme.

3.1.1. Intervention selection

Data were collected from 17 participants, 9 men and 8 women. Data from 4 participants were not included in the main data analysis as they were unable to adhere to the physical activity intervention and they did not have a percentage increase in exercise from week 1 to week 12. The remaining 13 participants included 7 men and 6 women with a mean (±SD) age of 61.4±8.4 years, BMI of 32.6±6.8 kg/m^2 and an AHI of 21.9±7.4 events per hour. Ethical approval was given by the Science, Technology, Engineering and Mathematics Ethical Review Committee at The University of Birmingham.

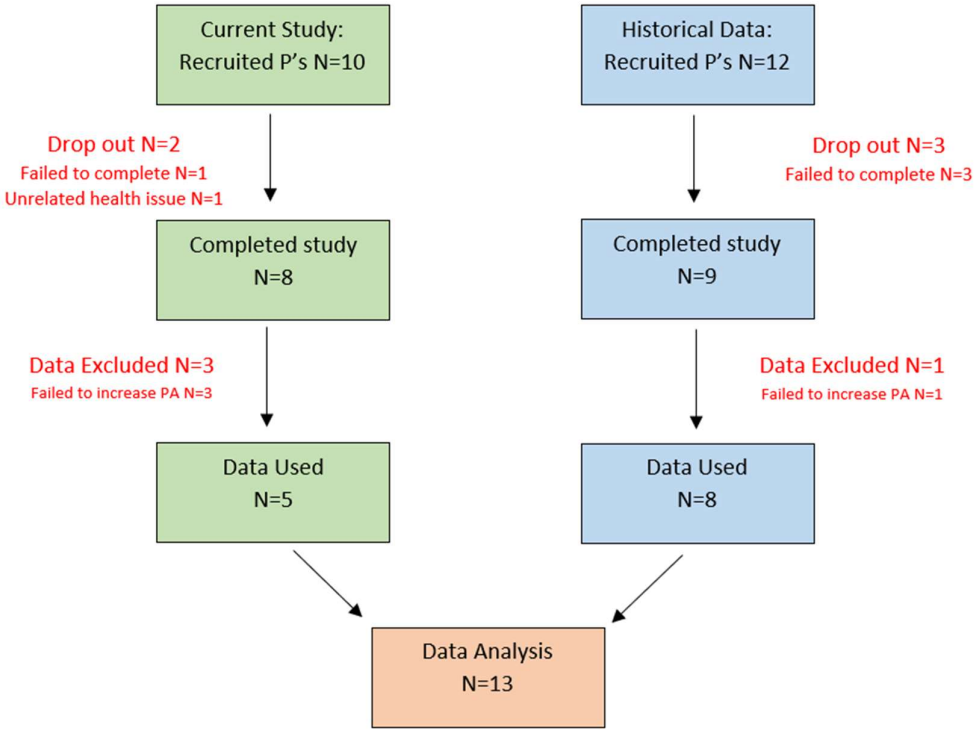

Figure 2. *Recruitment of participants flow diagram.*

3.2. Study Design and protocol

An intervention study was designed to test the effectiveness of a 12-week physical activity intervention to reduce the severity of OSA in people newly diagnosed with a moderate to severe form of the disease.

3.2.1. Screening

Initial screening tests were used to determine eligibility and establish a baseline for comparison. On arrival participants were fully informed about the study, given a chance to ask questions and signed informed consent. Basic health information questionnaires and the short form International Physical Activity Questionnaire (IPAQ) (Craig *et al.,* 2003) (See Appendix C) were completed, along with the Epworth Sleepiness Scale (Smyth, 2007) (See Appendix D). Anthropometric measures of height, using a laser measure (Bosch PLR 40C, Robert Bosch GmbH, Germany), weight and body composition, using electronic scales with bioelectrical impedance (The Ultimate Scale by Tanita Model 2000, Netherlands) and neck circumference, using a tape measure, were taken, represented by the first blue arrow on figure 3 below. BMI was later calculated.

3.2.2. Screening for the presence of OSA

Following initial screening, participants were asked to wear a domiciliary diagnostic Device (ApneaLink^{TM}Air, ResMed, San Diego, USA) on two consecutive nights, represented by the first red arrow on figure 3 below. The first night was for familiarisation with the device and no data were obtained. Results from the second night revealed the Apnoea-Hypopnoea Index (AHI) and determined eligibility to continue the study. Participants were excluded if their AHI was below 15, or if their results suggested that their apnoeic episodes were central in origin instead of obstructive. This is differentiated by the presence of respiratory effort during an apnoeic event, which is suggestive that the event is obstructive rather than central.

3.2.3. Physical Activity Intervention

Once participants were deemed eligible, a 12-week physical activity intervention began immediately. The activity programme included a gradual increase of physical activity. By week 12 all participants were involved in at least five x30-minute bouts of physical activity per week at a rate of perceived exertion (RPE) of 13 (See Appendix B). Borg's RPE scale is a numerical list with a range of 6-20 in which participants are asked to rate their whole body feeling of exertion (Williams, 2017). Participants were asked to report via text messaging, the

daily duration of exercise and RPE, to the researcher, along with daily units of alcohol consumed, represented by the green arrows in figure 3. During week 1, 6 and 12, participants wore an accelerometer (GT3X Actigraph, Pensacola, FL, USA), which provided subjective measure of the changes in activity and it was used to validate the self-reported measures, represented by the yellow arrows in figure 3.

3.2.4 Post-Intervention testing

The questionnaires and evaluation of OSA severity that were performed as part of the screening measures were repeated- post intervention- to give a comparison to the baseline, represented by the second blue and red arrow on figure 3.

3.2.5 Study design changes due to Covid-19 pandemic

During this study, social distancing practice was brought in and the University of Birmingham was shut due to the Covid-19 pandemic. This affected the way that data was collected from 7 out of the 8 patients that completed this intervention. Face to face contact with participants was not allowed, which meant that all equipment was posted to participants and video calls were utilised when explanations of equipment use were needed. Participants were instructed on how to record all anthropometric measures and provided with the correct equipment so that this data was taken by self-report.

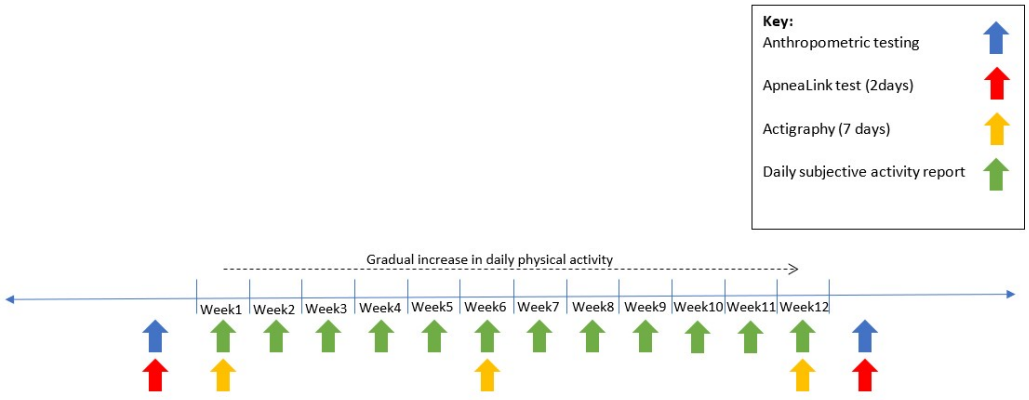

Figure 3. *Schematic representation of all measures being taken throughout study.*

3.3. Measures

3.3.1. Subjective physical activity

The short form IPAQ was used to measure habitual exercise in the seven days prior to the study and the final week of the intervention. IPAQ questionnaires are known and accepted as a means of recording repeatable and valid data having been used in 12 different countries among adults from 18 to 65 years old (Craig *et al.*, 2003).

3.3.2. Percentage increase in daily physical activity

Intensity of physical activity perceived by the participants was measured by Borg's rate of perceived exertion scale. Borg's RPE is shown to be strongly correlated with heart rate and blood lactate levels during exercise; this correlation is not affected by how physically activity the participants usually are (Scherr *et al.*, 2013), making it a practical tool for monitoring activity intensity in this study. An RPE of 11-13 (low) is recommended for less active individuals but an RPE of 13-15 would still be classed as aerobic (Scherr *et al.*, 2013). This information was used to advise participants on how to start and then increase physical activity throughout the intervention. Current daily guidelines for exercise are thirty minutes of moderate to vigorous activity five days per week (Pescatello, Riebe and Thompson, 2014). Participants in the current study were asked to aim to reach this level of activity by the final week of intervention as this has been shown to be a safe way to manage OSA in older adults (Giebelhaus *et al.*, 2000). The suggested gradual increase for the physical activity intervention was as follows; week 1-4- three x10-15-minutes of PA at an RPE of 9. Week 5-8- four x15-20-minutes of PA at an RPE between 9-13. Week 9-12- five x30minutes of PA at an RPE of 13.

3.3.3. Obstructive sleep apnoea

The ApneaLink^{TM} Device was used to detect severity of OSA in participants. ApneaLink home testing is seen as a reliable and easy-to-use tool for testing severity of OSA. Studies have shown that, at a cut-off point of AHI $\geq$ 15, the device has a sensitivity of 92-100% (Clark, 2009; Crowley, 2013) when compared to polysomnography results. Severity of OSA was based on AHI, where an AHI 5-15 is classed as mild, 15-30 as moderate and $\geq$ 30 as severe (Flemons W.W., 1999). An apnoea event is defined as the cessation of airflow for at least 10 seconds, whereas hypopnoea can be defined as a 30% reduction in airflow for 10 seconds with a 4% reduction in blood oxygen saturation, or a 50% reduction in airflow for 10 seconds with a 3% reduction in blood oxygen saturation (Al Lawati, Patel and Ayas, 2009).

3.3.4. Objective physical activity

Actigraph monitors were used to objectively measure physical activity and validate self-reported activity. The GT3X accelerometer has been found to accurately estimate free-living physical activity in most types of human activity (Santos-Lozano *et al.*, 2012). As suggested by Cain KL and Geremia CM, (2011), participants wore the monitor on their right hip, for seven days and for at least ten hours per day. Using the activity count per minute from the actigraph monitors, intensity of activity could be determined, with the cut-off points of 0-100, 191-1952, 1953-5724, 5725+ for sedentary, light, moderate and vigorous activity respectively (Freedson, Melanson and Sirard, 1998). 'Activity count' on an accelerometer is a measure calculated by detecting body motion and assessing acceleration which is converted and summed over a specified period of time (Freedson, Melanson and Sirad, 1998).

3.3.5. Sleepiness

Daytime sleepiness is commonly associated with OSA. This was tested using the Epworth sleepiness scale. This measure is shown to have a high level of internal consistency, and high validity and reliability for testing daytime sleepiness (Smyth, 2007).

3.3.6. Anthropometric Measures

BMI and weight were monitored as obesity is a risk factor for OSA (Al Lawati, Patel and Ayas, 2009), therefore reduction in BMI or weight could be a cause of reductions in AHI instead of physical activity. Body composition was measured using bioelectrical impedance analysis (BIA). Tanita BIA machines have been found to have high reliability in both men and women (Vasold *et al.*, 2019). However, the results given by BIA can be affected by confounding variables like hydration status (Petrie, 2004). Consequently, neck circumference is also an important measurement in case body composition changes are not detected. It is significantly correlated with both BMI and body fat percentage and can be used as an assessment of obesity (Coutinho, 2014). However, in order to minimise the influence of confounding factors, body composition measurements were performed as consistently as possible, at the same time of day and before a meal.

3.4. Data Analysis

Data analysis was performed using IBM SPSS statistics software version 25. The relationships between variables at baseline were assessed using Pearson's correlation

coefficient. Paired samples T-tests were employed to assess changes in variables over the intervention including anthropometric, and outcome measures. Self-reported exercise was calculated by multiplying the time spent exercising by the RPE reported for that bout of exercise and combining all physical activity sessions for the week together. The percentage change was calculated between week 1 and week 12. Repeated measures ANCOVA tests were used to check for confounding variables including weight, BMI and body fat percentage. A mixed-design ANOVA was used to test for differences between participants when split into two groups (i) Those that had a percentage increase in physical activity over the intervention and (ii) Those that had a percentage decrease in physical activity over the intervention. Significance was assumed where $p \leq 0.05$.

4. Results

4.1. Descriptive statistics

Data from 13 participants were included in the data analysis (6 females, 7 males). Individual data is presented in table 1. This indicates that the participants were obese with moderate OSA. Median alcohol intake was reported at a frequency of 1-2 times per week and 10-20 units.

			Pre-Intervention			Post-Intervention		
P. No.	M/F	Age (years)	Weight (Kg)	BMI	AHI (events/hour)	Weight (Kg)	BMI	AHI (Events/hour)
1	M	61	126.2	38.3	34.6	129	39	22.3
2	M	68	88	26.6	18	87.8	25.4	9
3	F	74	78.2	31.5	17.7	69.4	27.5	4.9
4	F	70	97.2	32.6	25.8	99.8	33.5	18.3
5	F	77	60.6	23.9	15.2	58.8	23.3	6.2
6	F	56	104	46.2	19	102	47	26
7	M	53	90.2	29.1	16.8	90	29	9.6
8	F	54	77	27.4	15	82	29	12
9	M	57	76	28	16.8	79	27.5	5.4
10	M	52	101	31.4	19.6	100	32	17
11	M	61	91	30	38.7	92	30	7.5
12	F	63	117	35	26	114.5	34.9	20.5
13	M	53	130	45	22	126.5	46.7	25
Mean		61.4	95.1	32.6	21.9	94.6	32.6	14.1
SD		8.4	20.4	6.8	7.4	20.6	7.5	7.7

Table 1. *Table of results for individual participants. Participant 1-5 was collected from the current intervention; Participant 6-13 is historical data.*

4.2. Baseline

Bivariate correlations were run to assess the relationships between variables at baseline. Pre intervention there was no significant correlation between AHI (21.9±7.4 events per hour) and BMI (32.6±6.8kg/m^2), p=0.36, R^2=0.07, or AHI and fat percentage (43.9%±15.1%), p=0.56 R^2=0.13. There was also no significant correlation between AHI and the amount of activity recorded by actigraphy in the first week of the intervention (410.4±165.4mins), p=0.54, R^2=0.04. There was however, a moderate and positive but non-significant correlation between AHI and weight (95.1±20.5kg), p=0.06, R^2=0.28. Additionally, when 1 outlier is removed from this, the correlation becomes significant and strong p<0.01, R^2=0.59.

4.3. Post intervention changes

Paired samples T-tests were used to identify significance of anthropometric changes pre- and post-intervention, as well as changes in outcome measures over the same time frame.

Figure 4 demonstrates that there were no significant changes in weight from pre-intervention (95.1±20.5 Kg) to post-intervention (94.6±20.6 Kg), p=0.76, or body fat percentage from pre-intervention (40.7%±10.8%) to post-intervention (39.7%±11.8%), p=0.45. Neck circumference from pre- (40±5.2 cm) to post- (39±5.9 cm) intervention and BMI from pre- (32.6±6.8 kg/m^2) to post- (32.6±7.5 kg/m^2) also had no significant change, p=0.35 and p=0.97, respectively.

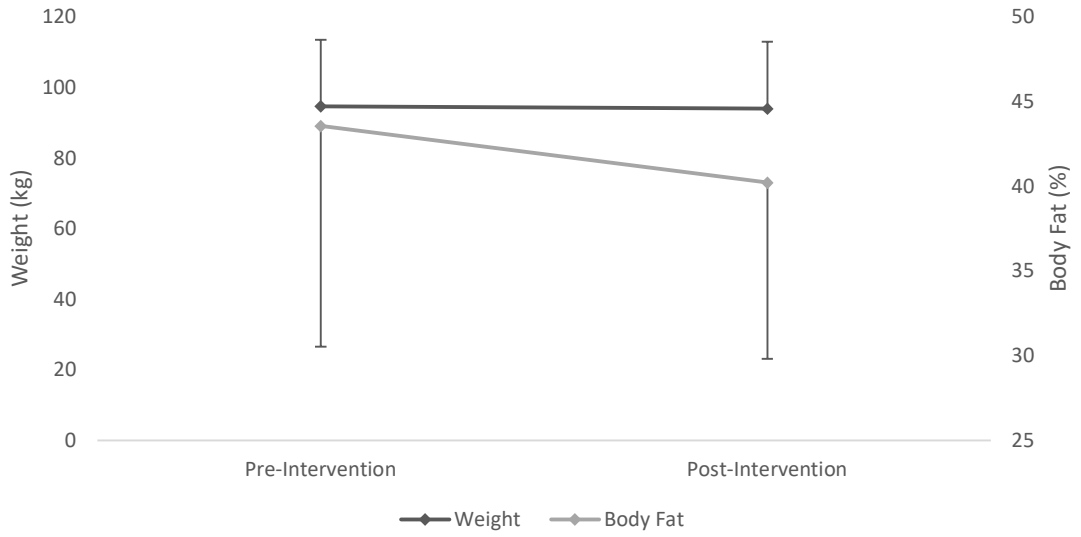

Figure 4. *Graph showing change in weight and body fat from pre- to post- intervention.*

The outcome measure for OSA severity was AHI, figure 5 demonstrates a significant reduction from pre- (21.9±7.4 events per hour) to post- (14.1±7.7 events per hour) intervention, $p<0.01$. Epworth sleepiness scale was used as an additional measure for OSA severity, however, there was no significant difference seen between the Epworth scores pre- (9.2±3.03) and post- (7±4.36) exercise intervention in this group, $p=0.07$.

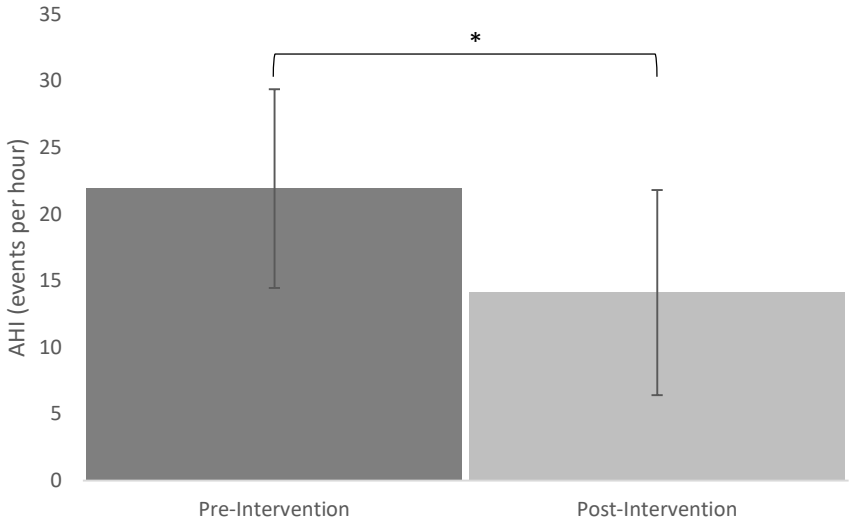

Figure 5. *Graph showing the mean(±SD) AHI of participants pre and post intervention. *Signifies a significant change p<0.01.*

Figures 6 and 7 represents the significant differences seen in self-reported physical activity measures from week 1 to week 12. Self-reported time spent exercising each week significantly increased from week 1 (224.5±233.7 mins) to week 12 (382.1±322.1 mins), $p<0.01$. Additionally, time spent exercising at an RPE above 12 significantly increased from week 1 (30.8±49.8 mins) to week 12 (220.1±140.3 mins), $p<0.01$, and the average RPE that participants exercised at also significantly increased from week 1 (10.6±1.5) to week 12 (13±1.7), $p<0.01$. However, actigraphy suggests that there was no significant difference in daily sedentary time when week 1 (731.6±137.6 mins) and week 12 (697.9±211.1 mins) were compared, $p=0.71$. The same was found for the difference in daily activity time from week 1 (410.5±165.4 mins) to week 12 (359.9±117.9 mins), $p=0.24$, as well as daily vigorous activity from week 1 (1.01±2.31 mins) to week 12 (1.9±2 mins), $p=0.30$ and weekly step count from week 1 (49550.8±11278.2 steps) to week 12 (46506.1±14981.9 steps), $p=-0.48$.

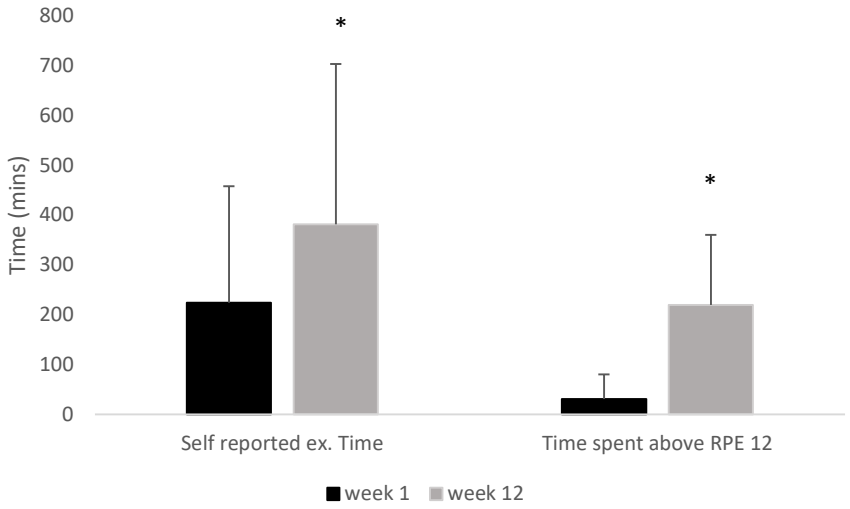

Figure 6. *Graph to show the mean (±SD) physical activity time and time spent above an RPE of 12 in week 1 and week 12 of the intervention. *represents a significant increase where P<0.01.*

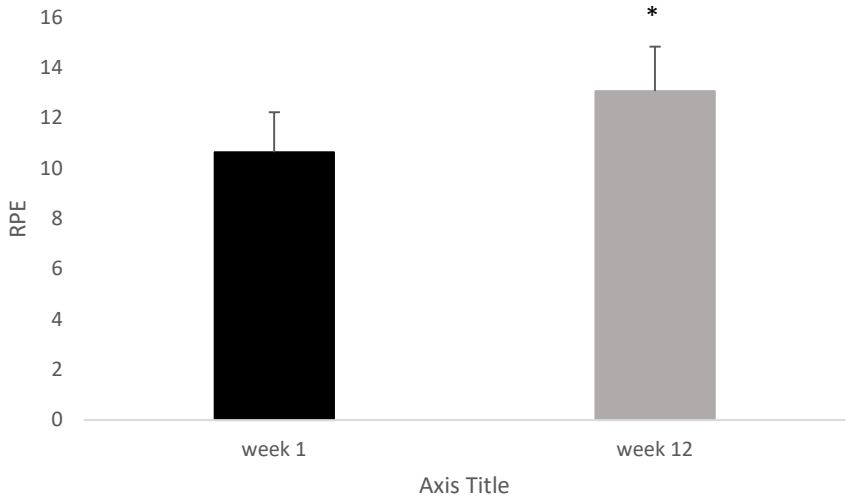

Figure 7. *Graph to show the mean (±SD) RPE in week 1 and week 12 of the intervention. *represents a significant increase where P<0.01*

Figure 8 represents that during week 1 there was a strong correlation between self-reported physical activity time and amount of activity measured by actigraphy (R^2=0.58), however this correlation dramatically decreased in week 12 (R^2=0.27).

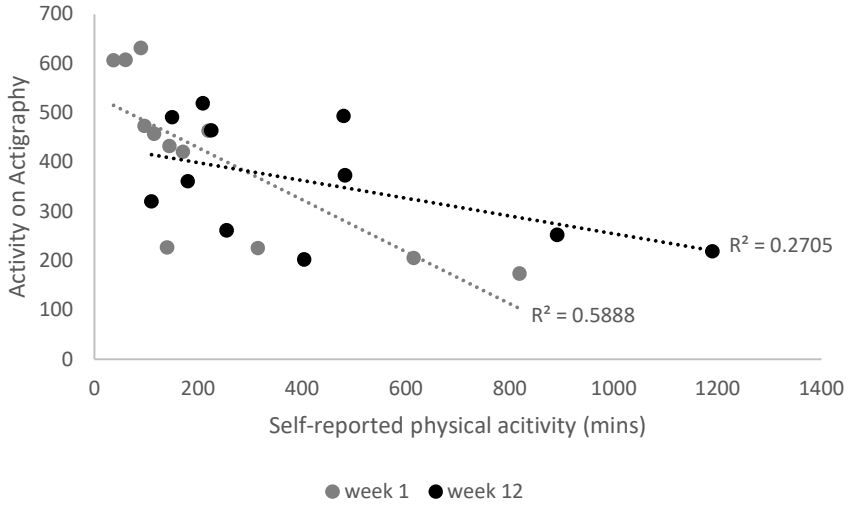

Figure 8. *The correlation between self-reported physical activity and activity recorded by actigraphy in week 1 and week 12 of the intervention.*

4.4. Severity of OSA and physical activity output

Figure 9 represents the medium to low but not significant correlation revealed by Pearson's correlation coefficient between change in AHI and percentage increase in exercise over the 12 week intervention ($r(13)=-0.222$, $p=0.466$). The R^2 for this correlation is 0.049, suggesting a week correlation so it is unlikely that the percentage increase in self-reported exercise can actually predict AHI reduction.

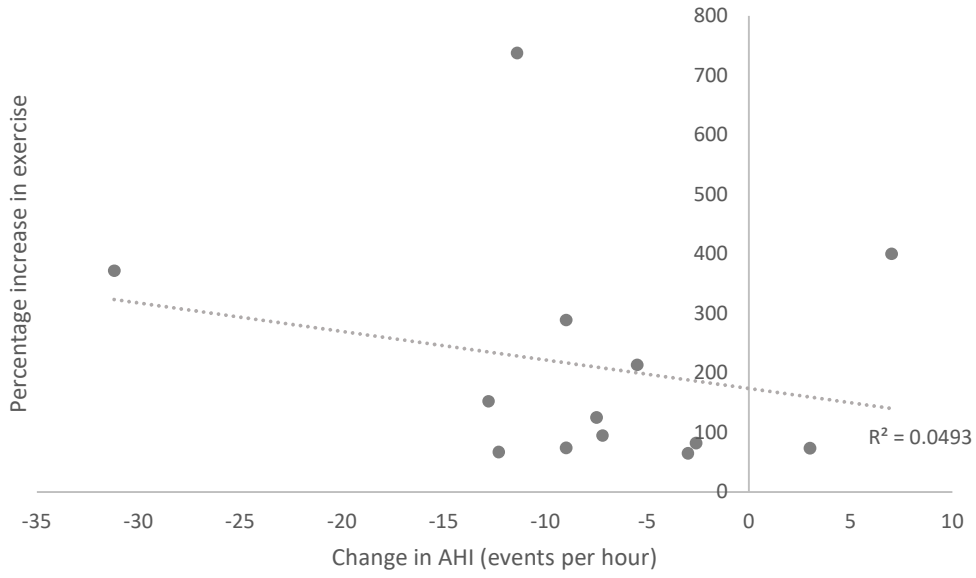

Figure 9. *Graph showing the correlation between change in AHI and % increase in exercise.*

4.5. Confounding variables

As previously stated, there was a significant reduction in OSA Severity (AHI) from baseline to end of intervention (see figure 5). In order to test for confounding variable effects of BMI, weight, and body fat percentage on the reduction of OSA severity, repeated measures ANCOVA tests were performed to examine each possible confounding variable. The results showed that there was no significant interaction between the change in severity of OSA and the change in weight, $p=0.65$. There was no significant interaction between change in severity of OSA and change in BMI, $p=0.19$. However, there was a significant interaction between change in severity of OSA and change in body fat percentage, $p<0.01$, figure 10 represents these changes.

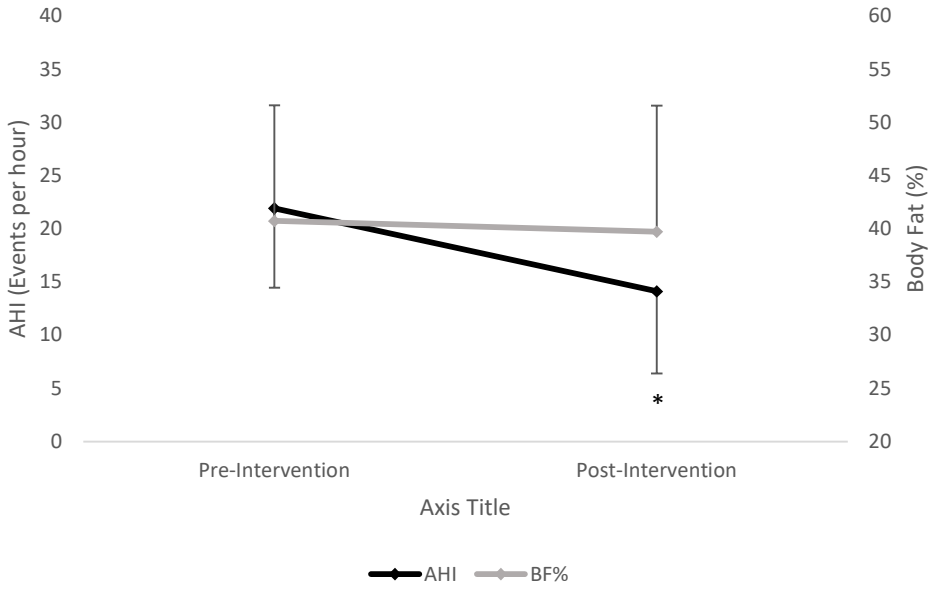

Figure 10. *Graph showing the mean (±SD) AHI and BF% pre- and post- intervention. *Represents a significant decrease from Pre- to Post- intervention where P<0.01.*

5. Discussion

An investigation into the ability of a 12-week unsupervised physical activity intervention to reduce the severity of OSA was carried out. Results showed a significant decrease in OSA severity and a significant increase in self-reported physical activity time and intensity, together with a significant interaction between change in OSA severity and change in body fat percentage. From personal research, it appears that the only other study looking at

manipulating duration and intensity of unsupervised physical activity to reduce OSA was carried out as a feasibility study in a group of older adults (Black, Whittaker and Balanos, 2018). This article concluded that unsupervised PA should be a focus for treatment of OSA. Additionally, Jurado-Garcia *et al.*, (2020), studied a 6-month gradual walking programme to reduce OSA severity and found similar results to this present study, although a significant reduction in BMI was also reported. The current study has built on these findings to show that a reduction in BMI is not necessary to reduce severity of OSA during a physical activity intervention.

Although the current study found an increase in self-reported physical activity, this was not supported by an increase in the participants activity when measured objectively by actigraphy. On the other hand, the, non-significant, but mean increase in vigorous exercise recorded by actigraphy does suggest that the intervention perhaps encouraged an increase in more structured and intense activity. This suggestion is also supported by the self-reported increase in RPE that was also recorded. This trend may have been more significant if the cohort had been larger, and this could be addressed in future research. A range of self-report methods for physical activity have been shown to be valid and reliable, especially in more vigorous activity (Ainsworth, Jacobs, and Leon., 1993; Kurtze *et al.,* 2008; RAUH *et al.,* 1992), this may explain the increase in self-reported activity and increase in vigorous actigraphy. However, this does not explain the reduction in correlation between self-reported PA in week 12 compared to week 1. The increase in more vigorous activity and lack of increase in overall activity measured by actigraphy may be explained by the national lockdown restrictions enforced on participants during the study. It is likely that participants were moving less during the day but taking part in more vigorous activity in the short period of time that they were allowed to leave their homes each day. This could have been perceived to be an increase in activity and was therefore reported it as such. It is also important to acknowledge that the actigraphy data is a snapshot of a short period of the intervention which may differ to the more prolonged changes that may be represented by the self-report. Additionally, the 'Activitystat hypothesis' is a potential factor that may have contributed to why daily activity measured by actigraphy did not significantly increase. The activitystat hypothesis suggests that if vigorous physical activity is increased other daily movement will have a compensatory decrease (Gomersall *et al.,* 2013). This is supported by evidence showing that in a group of participants with a similar mean age to that of the current cohort, a 12-week moderate physical activity training programme had no effect on total physical

activity time measured by accelerometery, suggesting that training activity was compensated for by a reduction in non-training physical activity (Meijer, Westerterp and Verstappen, 1999). Furthermore, in another study in a similar cohort, daily energy expenditure was measured using indirect calorimetry during a 14-week training programme. It was found that daily energy expenditure remained constant from pre to during the intervention due to a compensatory decrease in energy expenditure from free living activities (Morio *et al.,* 1998). With all this considered, due to the significant reduction in OSA severity and significant increase in self-reported physical activity and intensity, supported by actigraphy data showing an increase in vigorous activity, it has been concluded that this data supports the hypothesis that an increase in physical activity can reduce the severity of OSA and that this reduction is seen independently of weight loss and change in BMI, and we acknowledge that there may be a threshold of intensity of PA to lead to these changes, but further research is necessary to determine this.

These findings are further supported by some previous research where physical activity was found to be a safe and effective way to manage moderate to severe OSA (Giebelhaus *et al.*, 2000), but the current study adds further to these findings for it shows that the OSA severity, measured by AHI, can effectively be reduced during a physical activity intervention. The previous study used the respiratory disturbance index (RDI) as a measure of OSA severity instead of AHI which makes it harder to compare to other research as it is less common to report OSA severity in this way and unlike the current study it used a supervised exercise program. Other supervised exercise programs have been shown to be a beneficial management tool for OSA as they are able to reduce AHI in people with moderate to severe and undiagnosed OSA. For example Kline (2011), used a 12 week intervention including 150 minutes of moderate aerobic exercise and 2 resistance session per week and reductions in AHI were reported. The current study shows that an unsupervised physical activity program can have comparable effects to that of a supervised program as OSA severity can be reduced. This is a particularly important finding concerning the use of PA as a treatment for OSA for two primary reasons. Firstly, it would reduce the cost of running such interventions on a larger scale. Secondly, it could reduce time constraints for participants which could increase uptake and adherence to the treatment. However, it does not provide a concrete treatment plan for patients with OSA as there were still participants that dropped out of the intervention and others that were unable to increase their physical activity levels, on top of this further research is necessary to explore the threshold of PA necessary to elicit changes. Additionally,

only 9 of the 13 participants achieved the minimal clinically important change in AHI, which is 5 (Kim *et al.,* 2017).

It is important to see that meta-analysis by Mendelson *et al.* (2018), showed a significant decrease in AHI following an exercise intervention that was independent of BMI. Additionally, Van Offenwert *et al.* (2019) presented a negative correlation between PA levels and OSA severity by reviewing 7 previous studies that looked at correlations between OSA severity a physical activity measured by questionnaires, steps per day or activity sensors. Additionally, Kline *et al.*, (2014) states that there is a dose dependent relationship between physical activity and reduction in severity of OSA. However, although the current study presents data showing that over the 12-week physical activity intervention the participants increase their self-reported physical activity levels and they have a decrease in OSA severity, the current data do not support the dose dependant relationship as the correlation between percentage increase in PA and decrease in OSA severity was moderate but not significant. A greater or significant correlation to this effect may have been seen if a larger number of participants could have been recruited or a greater correlation was seen between self-reported physical activity and objective actigraphy data in week 12.

The current research contradicts Tuomilehto (2013), as their findings showed that AHI was only reduced in participants who showed a reduction in weight. However, this research was carried out over a 4-year period, and the current study has not looked at long term effects of PA beyond the 12-week intervention period. To do so could show a different outcome, but 2016 meta-analysis also found that exercise as a sole treatment for OSA is associated with improved clinical outcomes, such as reduced AHI (Aiello *et al.*, 2016), although this was not independent of BMI. This suggests that there are still inconsistencies in findings from studies that are using physical activity to reduce OSA severity and it is important to continue to study this area.

Further data analysis, highlighted in figure 11, compared the group of participants that adhered to the physical activity intervention with those who did not adhere to the intervention according to self-report. Those who did not adhere did not record a reduction in AHI over the 12-week intervention. This potentially provides a direct link between the reduction in OSA severity and level of PA increase needed to produce this reduction. However, this data is not statistically relevant due to the small sample size in the non-adherent group. A study with a larger group of participants could compare an intervention to a control group to produce

statistically relevant comparisons. Although the general consensus of research into the ability of physical activity alone to reduce OSA severity remains inconclusive, the study findings suggest that physical activity could be an effective alternative treatment for OSA.

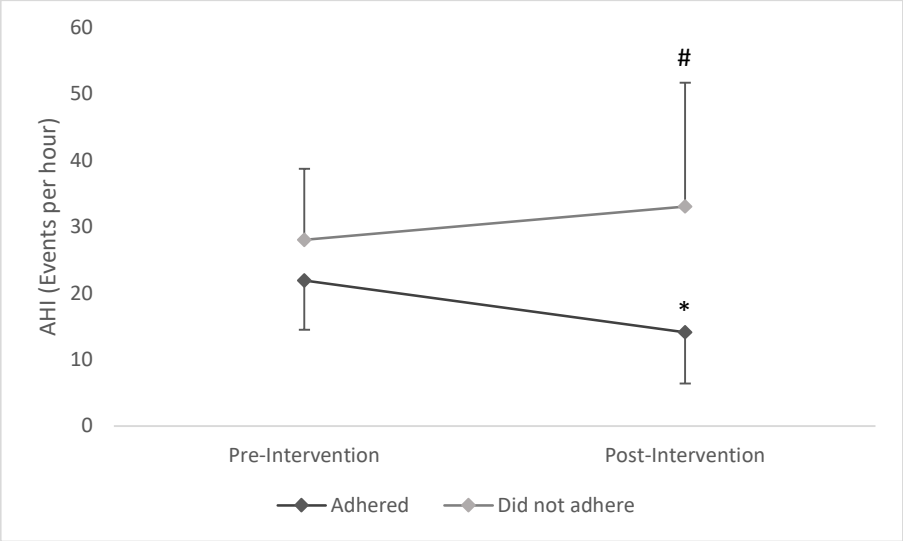

Figure 11. *Graph showing the mean AHI (±SD) of the two groups of participants, pre- and post- intervention. * Signifies a significant decrease in group from pre to post intervention. # Signifies a significant difference between groups at that time point.*

Fatty Deposits in the Upper Airway

Whilst the present study was not an investigation into the mechanistic explanations for the reduction in OSA severity, the results can offer some indications as to why such changes are seen. Among other things, one cause of OSA could be anatomical differences in the upper airway of obese people. These include reduced lumen size and decreased contractile force of the upper airway muscles due to fatty deposits (Corgosinho *et al.*, 2020). Wolk, Shamsuzzaman and Somers (2003), suggest that obesity may be related to OSA because of the effect that deposition of fat has on the upper airway anatomy and airway function. This is supported by Anandam *et al.* (2013), who suggest that dietary weight loss can reduce AHI and attribute this reduction in OSA severity, in part, to the reduction of upper airway collapse from pharyngeal fat deposits and reduced airway resistance. A decrease in protective contractile force of the upper airway dilator muscles of OSA patients compared to control participants is well documented. A review by Pillar and Shehadeh (2008), explains that inspiratory dilator phasic upper airway muscles, such as the genioglossus, are activated

during inspiration to counteract collapse of the airway against negative pressure Therefore an individual's propensity for collapse during sleep depends on both their anatomy and the level of dilator muscle activity, known as the protective reflex, and suggests that muscle structure is altered where there are excess fatty deposits within the muscle which affects the muscle activation. Carrera *et al.* (2004), suggest that patients with OSA have an abnormal distribution of type 2 muscle fibres in the genioglossus compared to non-obese, healthy controls and this could be the cause of collapse. However, they do not say if this is related to fatty deposits in the muscle or an alternative mechanism. Moreover, Ryan and Love, (1996) studied the velopharynx, a structure of the upper airway, and found that OSA patients with a larger neck circumference, so suggesting greater fatty deposits in the upper airway, have a greater airway collapsibility during wake than those with a smaller neck circumference, which may predispose them to collapse during sleep. Additionally, it is argued that greater neck fat deposition in men compared to women could be the reason for the higher rate of OSA seen in this population (Whittle *et al.*, 1999).

With this in mind, this current research showed a significant interaction between change in severity of OSA and change in body fat percentage. It could therefore be suggested that a contributing mechanism for reducing the severity of OSA could be a change in body composition including an increase in muscle and/or a reduction in fat, which can occur without a change in overall body weight. Further research is necessary to determine if fatty deposits specifically in the neck are directly affected by physical activity intervention and subsequently lead to a reduction in OSA severity. The current study cannot support this theory further as no significant changes in neck circumference in the participants were seen and fatty deposits in the neck were not measured directly, but it is recommended that this be considered in future research.

Upper Airway Muscle Strength

It is also important for, upper airway muscle strength to be considered as a contributing factor to OSA severity and upper airway muscle strength may also be affected by change in body composition. Type 2 diabetic patients with OSA have reduced inspiratory muscle strength compared with gender and age matched controls (Rehling *et al.*, 2017). Similarly, in a group of heart failure patients, those with sleep disordered breathing were found to have lower muscle strength (Bekfani *et al.*, 2020), however, skeletal muscles were measured in this study

by the handgrip dynamometer test and leg extension test so it cannot be directly compared to respiratory or upper airway muscle strength, but could be suggestive of overall muscle strength. If muscle strength of the upper airway dilator muscles could be improved with physical activity, airway collapse may be less likely during sleep. Inspiratory muscle training, such as breathing exercises, is a widely researched field and has been suggested as an adjunct for managing OSA (Hsu *et al.*, 2020) as it can reduce AHI by improving upper airway strength (Lin *et al.*, 2019). Oropharyngeal exercises have been seen to have a similar effect (Guimarães *et al.*, 2009). With this in mind, exercise may be achieving similar effects to upper airway training by improving muscle strength in the upper airway dilator muscles. For example, during exercise the prolonged and sustained increase in ventilation would act as a training mechanism for the respiratory muscles, and the increased amount of negative intrathoracic pressure during this time may increase strength of the upper airway muscles, such as the genioglossus. This suggestion is supported by a study which found that older adults who participated in habitual exercise had better respiratory muscle strength compared to those who did not (Mark *et al.*, 2005). Although respiratory muscle strength and strength of the upper airway muscle was not directly measured in the current study, the significant interaction between reduction in AHI and body fat percentage that was recorded could lead us to assume that a decrease in body fat percentage may be associated with an increase in muscle volume and therefore strength.

This assumption leads to the suggestion that further research is needed to measure the muscle strength in the upper airways pre- and post-physical activity intervention and so determine if this is a factor affecting the reduction in severity of OSA which is seen after physical activity intervention. Electromyography (EMG) could be used to measure muscle strength by measuring the level of recruitment and contractile force of the upper airway muscles. A method of measuring muscle strength of the genioglossus using EMG signals from a specially made gum shield has been previously used and could be effectively utilised for this kind of research (Griffin *et al.*, 2019).

Upper airway stimulation (UAS), in the form of hypoglossal nerve stimulation, has previously been trialled as a treatment for OSA. Some success has been seen in patients with a BMI below 40 (Weaver *et al.*, 2014). During this study UAS was used during sleep to prevent airway collapse rather than as a training method. However, a similar reduction in AHI was recorded the night after UAS to that of the reduction in AHI seen on the initial

nights when it was used. This suggests that residual lasting effects could occur using UAS as a training method and should be considered for trials as a treatment for OSA. Studying upper airway stimulation would be of considerable importance as it would allow researchers to record the effect of muscle activation to improve strength alone, without additional exercise effects, like changes in inflammatory profiles, which could be confounding.

Activity of the Upper Airway Muscles

It has been shown that, during wake OSA patients have greater activity in the genioglossus muscle. It is likely that this is due to the increased need for muscle activation to prevent collapse against a compromised airway anatomy which has increased negative intrathoracic pressure. However, at sleep onset, patients with OSA have a greater reduction in upper airway muscle activity, measured by EMG, than the healthy controls (Fogel *et al.*, 2005). Malhotra and White, (2002), agrees with this and states that the patency of the upper airway is preserved by activation of the genioglossus muscle, but even in healthy people the ability of the pharyngeal dilator muscles to maintain this patency is attenuated during sleep. Snoring and respiratory disturbance events, including apnoea and hypopnoea's, can be reduced if transcutaneous electrical stimulation is applied to the genioglossus muscle during non-rapid eye movement sleep as it reduces the ventilatory load by increasing muscle activity and maintaining airway patency (Steier *et al.*, 2011). However, longer lasting effects of this kind of treatment are not reported in the article. Previous research suggested that stimulation of the gastrocnemius muscle can increase the activity in the genioglossus and other muscles related to breathing which leads to an increase in minute ventilation up to 250% of normal values (Hussain *et al.*, 1991). The article concludes that stimulation of the limb muscle afferents can increase activation in the upper airway muscles leading to a reduction in airway resistance. Another study supported this by suggesting that stimulation of the sciatic nerve was associated with activation of the upper airway dilator muscles which then persisted after the cessation of stimulation (Haxhiu *et al.*, 1984). This could suggest that physical activity in which these skeletal muscles or nerves are stimulated, may reduce upper airway collapse during sleep due to the lasting increase in activity of the upper airway muscles rather than an increase in muscle strength specifically. It must be recognised that, both Hussain *et al.* (1991) and Haxhiu *et al.* (1984) studied this effect in anaesthetised dogs and it is therefore hard to generalise to a human population. However, Giebelhaus *et al.* (2000), studied heathy human

adults and found that physical activity engages the pharyngeal and glossal muscles which may suggest that the same effect may be seen in humans. The current study reports the benefits of increasing the amount of physical activity that the participants took part in. This physical activity could have stimulated the gastrocnemius muscle and/or sciatic nerve which could have had prolonged stimulating effects on the upper airway dilator muscles leading to improved patency of the upper airway and therefore a suggested cause of the reduced OSA severity that is reported. Suggestions for future research to test this theory would be to measure upper airway muscle activity before, during and after single bouts of exercise, as well as long term lasting effects to see if this correlates with the reduction in OSA severity that should be seen after physical activity.

Sleep State

It is important to emphasise the importance of sleep state to the presence of OSA. Even people with severe OSA do not have obstructive events during wake. Malhotra and White, (2002) suggest that during sleep there is a loss of neuromuscular reflex which is responsible for the activation of the genioglossus in response to negative pressure to prevent airway collapse. Another suggestion by Haxhiu *et al.*, (1984) is that decreased input from muscle afferents during sleep could be the cause of a reduction in the activity of upper airway muscles which leads to obstruction. OSA is less severe in slow wave sleep, but OSA patients tend to take longer to achieve slow wave sleep. Once this state is reached 57% of participants with OSA in a study had an AHI below 5 (Ratnavadivel, 2009). It has been shown that repeated exercise can cause a 33% increase in slow wave sleep (Aritake-Okada *et al.*, 2019) which could be a reason for the reduction in OSA severity. Similarly, in the current study the increase in physical activity over the 12-week intervention could have increased the amount of slow wave sleep which was achieved by participants which could have led to the reduction in OSA severity that was reported, however this was not tested directly due to not having the correct technology available. Nevertheless, further research is needed to establish a true correlation between a physical activity programme, sleep state and AHI in OSA patients. It could also prove useful to investigate and discover the true reason behind the reduction in genioglossus activity during sleep in comparison to wake, as it may lead to further treatment possibilities.

Regulation of breathing

Under normal conditions breathing is regulated by the autonomic nervous system in which the respiratory central pattern generator distributes rhythmic excitatory patterns to necessary muscles (Rice *et al.*, 2011). This includes rhythmic contraction of the tongue muscles, like the genioglossus (Cifra, Nani and Nistri, 2011). However, it is suggested that people with OSA tend to have poorly coordinated upper airway muscles (Brown *et al.*, 2013). The same article describes an 'en bloc' movement pattern that is seen in people with an AHI <5 which involves anterior movement of the whole posterior tongue during inspiration (P=0.002) which was measured by an MRI technique called Spacial Modulation of magnetization. They found that AHI was negatively correlated with total lateral wall movement during inspiration p=0.006 and subjects with an AHI of >30 were more likely to have a minimal movement pattern in which the tongue moved less than 1mm during inspiration. Additionally, no participants with severe OSA showed the focal oropharyngeal movement typical of normal healthy participants. This article suggested that the lack of movement may be a sign of motor neuropathy in OSA patients that is present even during wake. Many different breathing retraining techniques could affect the neuroplasticity of breathing control and improve the pattern of breathing as well as the strength of the respiratory tract (Courtney, 2020). For example, unlike other wind instruments, playing a double reeded instrument has been shown to reduce the risk of OSA (Ward, York and McCoy, 2012). This could be due to the specific muscles stimulated whilst playing these instruments. Oliven *et al.*, (2020), emphasises the importance of muscles that control tongue protrusion to improve OSA. This evidence suggests that if exercise stimulates the correct muscles the reduction in OSA severity could be linked to a change in the autonomic nervous system and the contraction of upper airway muscles. A stronger upper airway may be more coordinated and have more profound movement patterns which could therefore reduce the likelihood of collapse during sleep. The reduction in OSA severity that was seen in the current study could therefore be attributed to improved coordination of the upper airway like changed in the movement patterns of the tongue during inspiration. The evidence suggests that if the physical activity that the participants were doing promoted tongue protrusion this could be mechanism for the reduction in OSA severity. Future research would need to analyse the movement patterns of participants before and after a physical activity intervention to see if changes correlated with the reduction in OSA severity. It would be beneficial to also compare different modes of

activity and exercise so that patients could be given guidelines on how best to treat their OSA.

Fluid Shift

The mechanisms above could relate to the interaction between reduction in AHI and body fat percentage that was measured in this study. However, other suggested mechanisms rooted in published research papers that could lead to the reduction of OSA severity after exercise but were not investigated in this study include the potential that fluid shifts and inflammation improve as a result of exercise. Prolonged sitting or sedentary behaviour leads to an accumulation of fluid in the legs due to gravity. This fluid is then redistributed to the neck during sleep which increases the collapsibility of the upper airway and this shift of fluid correlates with increased AHI (Redolfi *et al.*, 2009). It is likely that fluid shift to the neck augments negative intrathoracic pressure by narrowing the airway due to excess fluid collecting in the pharyngeal walls and therefore increases the collapsibility (Redolfi *et al.*, 2015). The role of fluid in OSA is highlighted by the prevalence of OSA in fluid-retaining conditions, like heart failure, in which OSA is diagnosed in up to 44% of the population compared to the 9% that are diagnosed in the community population (White and Bradley, 2013). Increased daily step count can decrease fluid shift by augmenting musculovenous pumps in the legs to prevent the build up of fluid and decrease AHI (Redolfi *et al.*, 2015). It could be argued that other mechanisms driven by physical activity, like those discussed previously in this paper, could be the reason for the reduction in AHI. However, it is known that the use of compression socks can also have a similar effect on the reduction of fluid build-up and AHI (Redolfi *et al.*, 2011). Additionally the use of diuretics to decrease fluid retention in participants with severe OSA was able to decrease AHI, change in overnight leg fluid volume, and overnight change in neck circumference (Kasai *et al.*, 2014), suggesting that fluid shift is the mechanism rather than additional mechanisms prompted by exercise. However, Vena *et al.*, (2019) showed that stimulation of the calf muscle can reduce fluid shift and significantly reduce snoring, although this did not affect the severity of OSA that was measured. Additionally, it was suggested that if fluid shift was one of the driving mechanisms, then OSA should be worse in the second half of the night when fluid shift is at its maximum, but a study found that this is not the case so it is there-for unlikely to be a major contributing factor (Jafari and Mohsenin, 2011) and therefore it is likely that previously mentioned mechanisms are the cause of the reduction in OSA severity that was found in the current study rather than fluid shift. However, Jafari and Mohsenin, 2011,

studied the Breathing Disturbance index (BDI) rather than AHI so it is hard to compare this to other research, furthermore they only looked at the BDI in non-rapid eye movement sleep and obstructive Apnoea's and Hypopnoea's are much more severe in rapid eye movement sleep cycles (Mokhlesi and Varga, 2018).

Inflammatory Profiles

Finally, inflammatory profiles in OSA patients is a suggested mechanism for OSA in the literature. OSA patients have elevated levels of C-Reactive Protein (CRP), tumour necrosis factor alpha (TNF-α) and interleukin 6 (IL-6) which are associated with sleepiness and fatigue (Alves *et al.*, 2013). The same article suggests that physical activity can reduce inflammatory profiles and OSA symptoms like excessive sleepiness as IL-6 increases after exercise and TNF-α is inhibited. Corgosinho *et al.*, (2020) agrees that IL-6 is a promising biomarker for OSA and the link between obesity and OSA is the increased levels of CRP in these populations. Elevated levels of these proteins are linked to a chronic pro-inflammatory state that is present in patients with other conditions like obesity and type 2 diabetes. Additionally, Huang *et al.*, (2020), found that serum irisin, which is known to supress pro-inflammatory cytokines in obese patients, has a significant correlation with AHI which is independent of both PA and BMI. However, not all research agrees that inflammation is a mechanism for OSA. Cavagnolli *et al.*, (2014) found that CRP levels were not significantly different between OSA patients and a sedentary control group at baseline or after an exercise intervention, however although 80% of the OSA patients in this study had a reduction in AHI this was not statistically significant. If AHI had been reduced significantly then maybe the same would have been seen for CRP. Similarly, a recent study found that an 8-week supervised physical activity intervention was not sufficient to alter the inflammatory profiles (TNF- α and IL-6) of moderate to severe OSA patients (Borges *et al.*, 2020), but AHI was not measured as an outcome to see if OSA severity was still reduced from this exercise. The research into inflammatory profiles and OSA remains inconclusive with the range of proteins still being considered and the evidence for other mechanisms like reduced fat deposits in the neck, improved upper airway muscle strength and increased activity in the upper air way muscles provide a more comprehensive explanation for the reason that OSA severity decreased in the participants in this study. An interaction between multiple proteins cannot be ruled out or even multiple mechanisms that may, as a combination, be causing OSA and be responsible for the reduction in severity that is seen after physical activity, but further research is necessary to conclusively say what the mechanism is that causes OSA severity to

be reduced after a physical activity intervention. Furthermore, further research into the different treatment options including, individual treatment effectiveness, the mechanisms behind symptom improvement, and population specific outcomes is necessary to provide the most effective treatment of OSA on a wider scale.

6. Limitations

This study is not without limitations. The small sample size makes the results difficult to generalise to a wider population. With a larger sample, a more specific analysis could have been done to investigate the effect of different intensities of physical activity or into how different age groups are affected. However, this new data can be used to guide further research into these areas as well as further mechanistic research. Secondly, due to the Covid-19 pandemic the recruitment of participants was halted due to university and government guidance and some data from already recruited participants could not be collected. In order to make the work already conducted up to this point useable, the university allowed post-graduate students to use historical data to supplement those already collected. It was decided to use similar data as long as they had not been used in a previous publication. The supplemental unpublished data that were used were from a previous pilot study from the same laboratory. This improved the analysis of the data and allowed better conclusions to be drawn by increasing the overall sample size, but slight differences in the way data were collected between the two studies provided limitations in the way variables were analysed. Finally, self-report was used as the primary measure for duration and intensity of physical activity, which is likely to be subject to recall bias and/or over reporting. However, actigraphy was used to validate the self-reported data which had a good correlation in week one and the weak correlation in week 12 may be due to the lockdown restrictions that came into place just before this recording. It is also important to recognise the strengths within these data. The participants were from a range of ages and both a mixture of men and women none of whom were undergoing any other treatment for OSA. This is important for generalisability of the findings. We were also able to compare values from the same group of people pre- and post- intervention to reduce the effects of individual differences and it allowed direct study of the hypothesis set out as well as giving suggestions for further research required in the area.

7. Conclusion

The current study supports the possibility that exercise rehabilitation can be used as a cost-effective method of treatment for obstructive sleep apnoea, as an adjunct or as an alternative for CPAP. This could improve the uptake and adherence to treatment of OSA or be used by those that cannot tolerate CPAP. This would lead to health benefits to the patients and in the future possibly reduce treatment costs to the NHS due to treating the implications of OSA. It has also provided useful insight into further research necessary for possible mechanisms of the disease. As the hypothesis predicted, the severity of OSA can be significantly reduced during an intervention with a gradual increase of physical activity over a 12-week intervention independent of a reduction in weight as the participants demonstrated an increase in self-reported physical activity and a decrease in OSA severity. Further research is needed in a larger cohort to explore the suggestion of a dose dependent relationship between increase in PA and OSA severity as no significant correlation was found between the two. Furthermore, no objective data is available from the current research to back up the self-reported increase in PA as no significant increase in physical activity is reported by actigraphy which may be the reason for the correlation being non-significant. Additionally, further research is needed to confirm the mechanism responsible for the reduction in OSA severity, but results suggest that the concentration of fatty deposits in the upper airway muscles and/or the level of activity and strength of this muscle group may be involved in the likelihood of the upper airway collapsing during sleep. In addition, further research is needed in order to determine a threshold for physical activity that would be enough to reduce the severity of OSA and provide better guidelines for patients that may use it as treatment. Furthermore, additional research is needed to determine the mechanisms causing OSA and exactly how physical activity reduces the severity of OSA as this could provide an important insight into potential treatments for the condition.

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Appendixes

Appendix A- Apnoea-Hypopnoea index scale

AHI as a measure of OSA Severity	
5-15 events per hour	Mild
15-30 events per hour	Moderate
≥30 events per hour	Severe

(Flemons W.W., 1999)

Appendix B- Borge RPE scale

Borg RPE	
Score	**Level of exertion**
6	No exertion at all
7	
7.5	Extremely light
8	
9	Very light
10	
11	Light
12	
13	Somewhat hard
14	
15	Hard (heavy)
16	
17	Very hard
18	
19	Extremely hard
20	Maximal exertion

(Borg, 1998)

Appendix C- International physical activity questionnaire

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE (August 2002)

SHORT LAST 7 DAYS SELF-ADMINISTERED FORMAT

FOR USE WITH YOUNG AND MIDDLE-AGED ADULTS (15-69 years)

The International Physical Activity Questionnaires (IPAQ) comprises a set of 4 questionnaires. Long (5 activity domains asked independently) and short (4 generic items) versions for use by either telephone or self-administered methods are available. The purpose of the questionnaires is to provide common instruments that can be used to obtain internationally comparable data on health–related physical activity.

Background on IPAQ

The development of an international measure for physical activity commenced in Geneva in 1998 and was followed by extensive reliability and validity testing undertaken across 12 countries (14 sites) during 2000. The final results suggest that these measures have acceptable measurement properties for use in many settings and in different languages, and are suitable for national population-based prevalence studies of participation in physical activity.

Using IPAQ

Use of the IPAQ instruments for monitoring and research purposes is encouraged. It is recommended that no changes be made to the order or wording of the questions as this will affect the psychometric properties of the instruments.

Translation from English and Cultural Adaptation

Translation from English is supported to facilitate worldwide use of IPAQ. Information on the availability of IPAQ in different languages can be obtained at www.ipaq.ki.se. If a new translation is undertaken we highly recommend using the prescribed back translation methods available on the IPAQ website. If possible please consider making your translated version of IPAQ available to others by contributing it to the IPAQ website. Further details on translation and cultural adaptation can be downloaded from the website.

Further Developments of IPAQ

International collaboration on IPAQ is on-going and an ***International Physical Activity Prevalence Study*** is in progress. For further information see the IPAQ website.

More Information

More detailed information on the IPAQ process and the research methods used in the development of IPAQ instruments is available at www.ipaq.ki.se and Booth, M.L. (2000). *Assessment of Physical Activity: An International Perspective.* Research Quarterly for Exercise and Sport, 71 (2): s114-20. Other scientific publications and presentations on the use of IPAQ are summarized on the website.

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think *only* about those physical activities that you did for at least 10 minutes at a time.

1. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling?

   _____ **days per week**

   ☐ No vigorous physical activities → ***Skip to question 3***

2. How much time did you usually spend doing **vigorous** physical activities on one of those days?

   _____ **hours per day**

   _____ **minutes per day**

   ☐ Don't know/Not sure

Think about all the **moderate** activities that you did in the **last 7 days**. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

3. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

   _____ **days per week**

   ☐ No moderate physical activities → ***Skip to question 5***

SHORT LAST 7 DAYS SELF-ADMINISTERED version of the IPAQ. Revised August 2002.

4. How much time did you usually spend doing **moderate** physical activities on one of those days?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

Think about the time you spent **walking** in the **last 7 days**. This includes at work and at home, walking to travel from place to place, and any other walking that you might do solely for recreation, sport, exercise, or leisure.

5. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time?

_____ **days per week**

☐ No walking → ***Skip to question 7***

6. How much time did you usually spend **walking** on one of those days?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

The last question is about the time you spent **sitting** on weekdays during the **last 7 days**. Include time spent at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television.

7. During the **last 7 days**, how much time did you spend **sitting** on a **week day**?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

This is the end of the questionnaire, thank you for participating.

SHORT LAST 7 DAYS SELF-ADMINISTERED version of the IPAQ. Revised August 2002.

(Craig *et al.,* 2003)

Appendix D- Epworth Sleepiness Scale Questionnaire

Epworth Sleepiness Scale

How likely are you to doze off or fall asleep in the following situations, in comparison to feeling just tired? This refers to your usual way of life in recent times.

Even if you haven't 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

It's important that you answer each question as best you can.

Situation	**Chance of Dozing (0=low, 3=high)**
Sitting and Reading	
Watching TV	
Sitting still in a public place (e.g. a theatre, cinema or a meeting)	
A passenger in a car for an hour without a break	
Lying down to rest in the afternoon when the circumstances allow	
Sitting and talking to someone	
Sitting quietly after lunch without having drunk alcohol	
In a car or bus having stopped for a few minutes in traffic	
Total	

(Smyth, 2007)