

## Chapter 1 Literature Review

### 1.1 Actigraphic Monitoring of Physical Activity

#### 1.1.1 Introduction

The idea of using actigraphic devices to noninvasively monitor human movement and activities has long been known. Both Leonardo da Vinci and Thomas Jefferson designed mechanical pedometers hundreds of years ago (Montoye *et al.*, 1996; Wolf, 1995). There have been great advances in actigraphic devices in recent years (Freedson *et al.*, 2012), which nowadays include not only pedometers and accelerometers, but also multiple sensor systems and accelerometers combined with heart rate sensors (Butte *et al.*, 2012; Chen *et al.*, 2012).

Berlin *et al.* (2006) argued that there are four reasons for assessing physical activity: 1) to determine if physical inactivity is a problem, 2) to establish goals to increase physical activity, 3) to provide incentives and evaluate whether physical activity has been increased, and 4) as an outcome measure for physical therapy interventions. Improvements in the performance of actigraphic devices now enable objective assessment of physical activity and allow prolonged monitoring of human activity under free living conditions for a range of clinical and sporting purposes in a manner that was not possible until recently, including the monitoring of existing functional disability in a range of clinical conditions and in evaluating therapeutic outcomes. However, data obtained from actigraphic devices are highly dependent on a number of factors, especially the device employed and the nature of the activity that is being studied. The aim of this chapter was to review the potential and demonstrated effectiveness of currently available actigraphic devices in clinical and sporting applications.

## 1.1.2 Historical Development of Activity Monitors

Two types of wearable electronic devices that have been widely employed for monitoring physical activity in free living environments are the pedometer which measures the number of steps taken, and the accelerometer which measures linear acceleration and deceleration. *Table 1-1* from Berlin *et al.* (2006) compares important features of these two types of devices. In addition to these, other devices have been used to monitor physical activity, including load transducers (foot contact monitors), heart rate monitors, combined accelerometers and heart rate monitors, and multiple sensor systems (Butte *et al.*, 2012).

*Table 1-1:* A comparison between the Pedometer and the Accelerometer (Berlin *et al.*, 2006).

	<b>Predometer</b>	<b>Accelerometer</b>
Monetary cost	Low (\$10–\$200)	Mid to high Computer interface=\$300–\$600 Unit=\$300–\$600
Primary outcome	Steps	Counts
Activity		
Type	Ambulatory	Lower extremity and trunk
Frequency	No	Yes
Duration	No	Yes
Intensity	No	Yes
Participant burden <sup>a</sup>	Low	Low
Investigator burden <sup>b</sup>	Low	Moderate
Data acquisition	Hand transcribed	Computer downloaded
Placement	Waist	Waist, wrist (least preferred), or ankle
Central obesity interferes with recording of activity	Yes	Possibly if worn on waist; not an issue if worn on wrist or ankle

### 1.1.3 Pedometers

Pedometers are small inexpensive devices that measure the number of steps taken and therefore have the potential to estimate the distance travelled during walking or running (Bassett *et al.*, 1996; Berlin *et al.*, 2006; Butte *et al.*, 2012; Freedson and Miller, 2000; Melanson *et al.*, 2004). Pedometers are typically attached to a participant's waist at the thigh's midline and work by detecting vertical movement during gait cycles (Berlin *et al.*, 2006; Schneider *et al.*, 2004). *Figure 1-1* from Consolvo *et al.* (2006) illustrates the Omron HJ-112 pedometer.



*Figure 1-1:* The Omron HJ- 112 pedometer (Consolvo *et al.*, 2006).

Pedometers are limited by a number of disadvantages. Significant inaccuracies have been noted in pedometer based measurements of the number of steps taken and the distance travelled (Bassett *et al.*, 1996; Crouter *et al.*, 2003; Melanson *et al.*, 2004; Schneider *et al.*,

2004). It is plausible that changes in stride length at different workload intensities contribute to inaccuracies in pedometer based estimates of distance travelled. In addition, pedometers do not measure the duration of an activity (Berlin *et al.*, 2006; Freedson and Miller, 2000) or the intensity of an activity (Berlin *et al.*, 2006), and are relatively insensitive to light activities and activities other than locomotion (Bassett *et al.*, 1996; Berlin *et al.*, 2006; Crouter *et al.*, 2003; Freedson and Miller, 2000; Melanson *et al.*, 2004).

#### 1.1.4 Accelerometers

Accelerometers are small, portable electronic devices that detect acceleration and deceleration (Berlin *et al.*, 2006; Butte *et al.*, 2012; Freedson and Miller, 2000). The data from accelerometers is automatically expressed in dimensionless units known as counts which are a measure of the intensity and frequency of acceleration and deceleration in one plane but are specific to each type of accelerometer (Berlin *et al.*, 2006). Early actigraphs were non-linear threshold motion detectors that typically failed to detect small movements (Ancoli-Israel *et al.*, 2003). Newer generation accelerometers such as the microelectromechanical system sensors combine improved sensitivity with improved microprocessor capabilities which include analog bandpass filtering and digitization of the signal with an analog to digital converter (Ancoli-Israel *et al.*, 2003; Chen *et al.*, 2012; Freedson and Miller, 2000). These features enable the newer generation accelerometers to measure both the amount and intensity of movement and thereby provide improved objective assessment of physical activities (Chen *et al.*, 2012; Freedson and Miller, 2000). Band-pass filtering of the signal can be useful for filtering out non physiological signals, although further research into this area is warranted (Ancoli-Israel *et al.*, 2003; Chen *et al.*, 2012).

Although more complex and costly than pedometers, accelerometers offer a number of distinct advantages and have gained widespread use in monitoring and quantifying body movement and physical activity. Unlike pedometers, accelerometers measure the intensity, frequency, pattern and duration of activity (Berlin *et al.*, 2006; Butte *et al.*, 2012; Freedson and Miller, 2000). Accelerometers also have the capacity for recording data over prolonged periods and the recorded data can then be downloaded onto a personal computer for analysis (Berlin *et al.*, 2006; Butte *et al.*, 2012; Freedson and Miller, 2000). Such analyses can provide useful features, including long term free-living estimates of body energy expenditure (BEE) (Berlin *et al.*, 2006). These devices can be worn on various parts of the body, including the waist, wrist, ankle or chest (Berlin *et al.*, 2006; Brage *et al.*, 2006; Zhang *et al.*, 2003). **Figure I-2** from Haug *et al.* (2000) illustrates a commonly used accelerometer actigraphic device, the Actiwatch, which is worn on the wrist.



**Figure I-2:** A illustration of a wrist mounted Actiwatch (Cambridge Neurotechnology) (Haug *et al.*, 2000).

Accelerometers detect motion in one or more planes, with uniaxial accelerometers usually sensing motion in the vertical plane, while biaxial and triaxial accelerometers sense motion in two or three planes positioned at 90 degrees to one another (Berlin *et al.*, 2006;

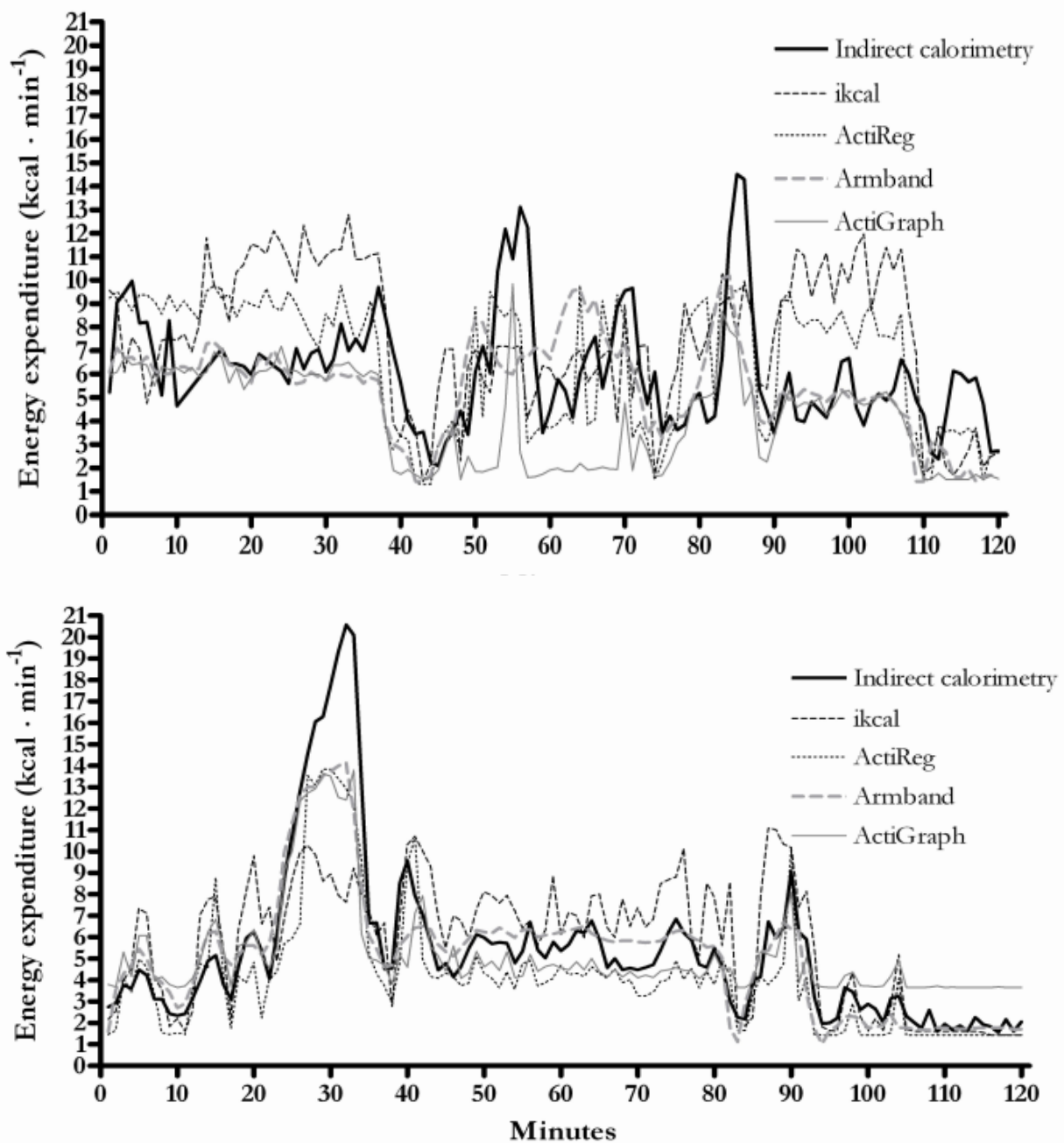
Butte *et al.*, 2012; Freedson and Miller, 2000). Triaxial accelerometers would on theoretical grounds seem to offer greater potential for capturing a broader range of body movements and thereby offer more accurate estimates of BEE than uniaxial accelerometers (Freedson and Miller, 2000). However, it remains unclear whether triaxial accelerometers provide more accurate assessment of physical activity than the generally cheaper uniaxial accelerometers (Berlin *et al.*, 2006; Eston *et al.*, 1998; Hendelman *et al.*, 2000; Welk *et al.*, 2000; Westerterp, 1999).

Although conferring distinct advantages over pedometers, accelerometers also have limitations (Bassett *et al.*, 1996; Brage *et al.*, 2004). Body energy expenditure is not a direct and straightforward function of accelerometer activity counts for all types of physical activity (Staudenmayer *et al.*, 2012). Moreover, no single regression equation appears to be capable of accurately predicting BEE from accelerometer data across the wide range of different types of body movements and activities that a person may encounter during their daily activities (Bassett *et al.*, 2000; Brage *et al.*, 2005; Brage *et al.*, 2004; Hendelman *et al.*, 2000). This limitation stems in part from the inability of motion sensors to detect static work and isometric contractions, or to accurately detect activities such as those involving carrying or lifting loads or travelling up inclines (Corder *et al.*, 2005; Ekelund *et al.*, 2001; Hendelman *et al.*, 2000; Meijer *et al.*, 1989; Thompson *et al.*, 2006; Westerterp, 1999).

Significant differences in step counts, accelerometer counts and estimated BEE occur when comparing different accelerometer devices (Balogun *et al.*, 1988; Bassett *et al.*, 2000; Berntsen *et al.*, 2010; Feito *et al.*, 2012; Hendelman *et al.*, 2000; King *et al.*, 2004), although similarities from different devices have also been reported (John *et al.*, 2010). **Figure 1-3** from (Berntsen *et al.*, 2010) illustrates the variability in estimated BEE from four different

accelerometers in free living studies. In addition, as has been commented on by many investigators, inaccuracies in accelerometer derived estimates of BEE are at least partly due to an inability to adequately detect motion because the accelerometer has been inappropriately positioned in relation to the type of body movement and type of physical activity being investigated (Bassett *et al.*, 2000; Boerema *et al.*, 2014; Bouten *et al.*, 1997; Corder *et al.*, 2005; Hendelman *et al.*, 2000; Westerterp, 1999; Yngve *et al.*, 2003). For example, wrist worn actigraphs may not adequately detect body trunk or leg movements and may result in erroneous underestimates of BEE during activities involving such movements. In contrast, waist worn accelerometers are sensitive to lower extremity and trunk movements during activities such as walking and running, but are less suited for upper extremity or seated activities (Berlin *et al.*, 2006). Consequently, the best position where an accelerometer is worn depends upon the type of activity that is to be monitored (Berlin *et al.*, 2006).

A number of approaches have been taken to address the dependence of accelerometer performance on where accelerometers are worn in relation to the type of activity being monitored and to improve the accuracy of actigraphic BEE estimates. Such approaches include the use of multiple accelerometers positioned at multiple sites on the body, and the combination of accelerometers and a heart rate monitor. The use of multiple accelerometers positioned simultaneously at multiple sites on the body has yielded disappointing results with little or no improvement in the accuracy of BEE estimates (Berntsen *et al.*, 2010; Swartz *et al.*, 2000). This is consistent with the lack of improvement in accuracy noted by Eston *et al.* (1998) when multiple pedometers were simultaneously worn on the ankle, hip and wrist. However, as will be discussed in detail in *section 1.1.7*, the combined accelerometer – heart rate approach has yielded superior accuracy in BEE estimates (Brage *et al.*, 2005; Brage *et al.*, 2004; Corder *et al.*, 2005).

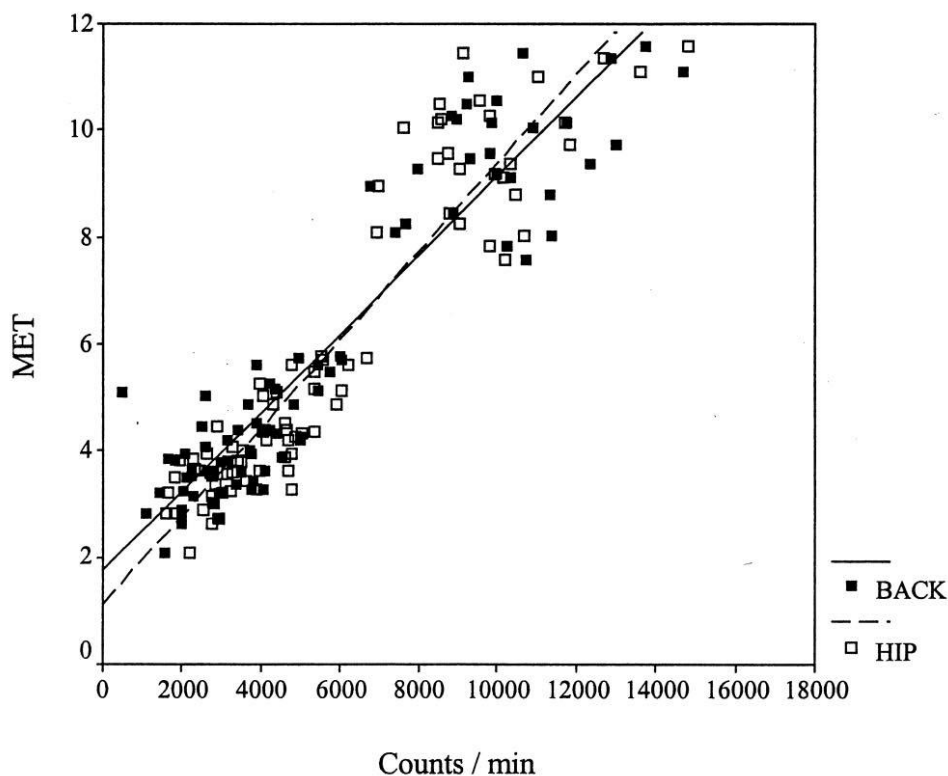


**Figure 1-3:** The differences in measurement between differing activity monitors and the variation in resulting energy expenditure (top- 32 year old male-walk, cycle and then walk for 40 minutes each; bottom -34 year old male-brisk walking 25 minutes, then 15 minutes of running, 30 minutes playing tennis, and 50 minutes carrying books and papers (Berntsen *et al.*, 2010).



### 1.1.5 Estimation of Body Energy Expenditure from accelerometers

Many studies have shown significant mathematical correlations between accelerometer activity counts and direct and indirect calorimetric measurements of BEE (Assah *et al.*, 2010; Barreira *et al.*, 2009; Bassett *et al.*, 2000; Bouten *et al.*, 1997; Bouten *et al.*, 1996; Brage *et al.*, 2004; Corder *et al.*, 2005; Crouter *et al.*, 2006; Crouter *et al.*, 2012; Ekelund *et al.*, 2001; Eston *et al.*, 1998; Hendelman *et al.*, 2000; King *et al.*, 2004; Meijer *et al.*, 1989; Puyau *et al.*, 2002; Swartz *et al.*, 2000; Warolin *et al.*, 2012; Welk *et al.*, 2000; Westerterp, 1999; Yngve *et al.*, 2003). *Figure 1-4* from Yngve *et al.* (2003) shows an example of the relationship between accelerometer activity counts and BEE measured by indirect calorimetry during walking and jogging on a treadmill.



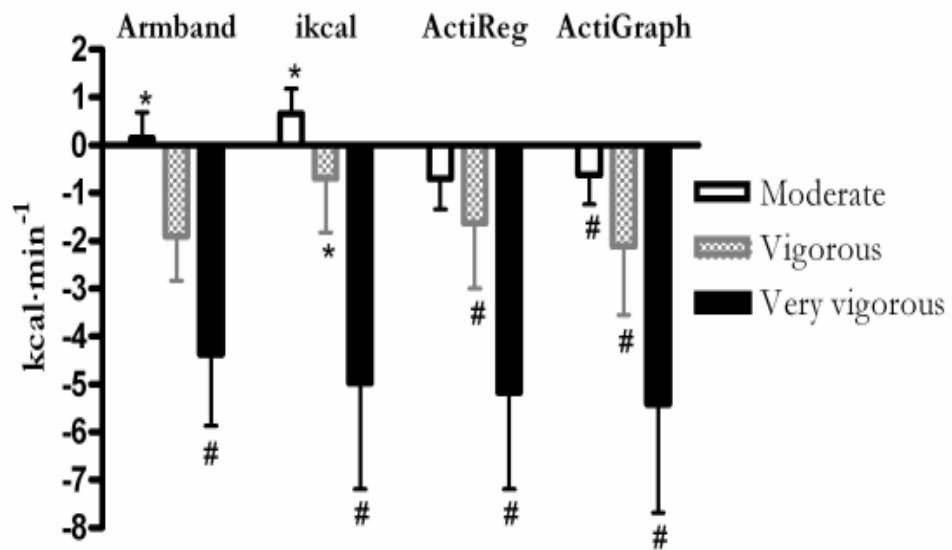
*Figure 1-4:* The relationship between accelerometer activity counts (positioned on the back and the hip) and body energy expenditure measured in metabolic equivalents (METs) by indirect calorimetry during treadmill walking and running (Yngve *et al.*, 2003).

Accelerometer monitoring can provide useful insights into physical activity patterns over sustained periods (Ainsworth *et al.*, 2000; Hansen *et al.*, 2012; Hinkley *et al.*, 2012; Riddoch *et al.*, 2007). However, there are significant limitations to using accelerometer based estimates of BEE as an alternative to more precise methods such as indirect calorimetry. First, the accuracy of BEE predictions predicted on the basis of accelerometer activity counts alone are considered to be unacceptably high (Zakeri *et al.*, 2008). In addition, the mathematical relationship between accelerometer activity counts and BEE on which correlations between accelerometer activity counts and BEE are based are typically only specific to the one or several types of physical activity investigated in each individual study. Indeed, as has already been discussed (refer to *section 1.1.4*), no single regression equation appears to be able to accurately predict BEE from accelerometer data across the wide range of different types of body movements and activities that a person may encounter during their daily activities. *Figure 1-5* from Berntsen *et al.* (2010) shows inaccuracies in estimated BEE from four different accelerometers in free living studies.

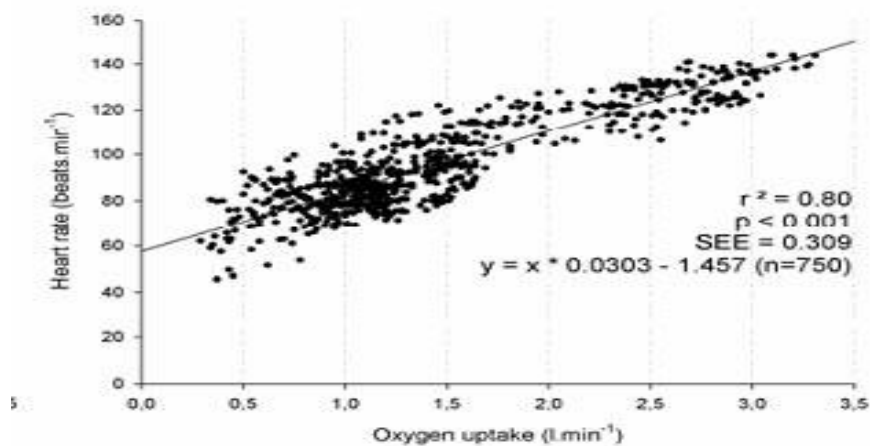
### **1.1.6 Estimation of Body Energy Expenditure from Heart Rate**

A fundamental principle in exercise physiology is that heart rate during physical exertion is directly and linearly related to oxygen consumption over a wide range of exercise workloads, and this relationship has long been used to obtain approximate estimates of oxygen consumption during exercise (Andre and Wolf, 2007; Astrand and Ryhming, 1954; Bragada *et al.*, 2009; Gastinger *et al.*, 2010; Rowlands *et al.*, 1997). *Figure 1-6* from Gastinger *et al.* (2010) illustrates the linear relationship between heart rate and oxygen consumption over a range of workloads. Using heart rate in this manner has the advantage that it can be readily monitored by small portable electrocardiograms. Heart rate monitoring

correlates well with behavioural observation of physical activity (Scruggs *et al.*, 2005) and can provide useful insights into physical activity patterns over sustained periods (Armstrong and Bray, 1991). However, there are limitations to using heart rate for estimating BEE which have hampered the utility of heart rate alone as a means of estimating BEE. First, investigators have noted that there is considerable individual variation in the relationship between heart rate response and exercise intensity (Brage *et al.*, 2005; Brage *et al.*, 2004; Livingstone, 1997). Second, the relationship between heart rate and exercise intensity is a linear at low levels of exercise such that heart rate overestimates BEE at low levels of exercise, an effect that has been attributed to factors such as anxiety (Andre and Wolf, 2007; Bussmann *et al.*, 2000; Corder *et al.*, 2005; Freedson and Miller, 2000; Livingstone, 1997; Livingstone *et al.*, 1992; Meijer *et al.*, 1989). In addition, the relationship between heart rate and oxygen consumption is affected by the type of exercise and body movements involved in the activity (Rowlands *et al.*, 1997). For example, arm exercise elicits higher heart rate responses than leg based exercise at equivalent workloads and levels of oxygen consumption (Taguchi and Horvath, 1987; Tulppo *et al.*, 1999; Vokac *et al.*, 1975).



**Figure 1-5:** Mean difference in energy expenditure between 4 accelerometer different motion sensors and indirect calorimetry during 3 levels of exercise intensity. A negative value indicates underestimation and a positive value indicates overestimation. \*  $p < 0.05$  and #  $p < 0.001$  (Berntsen *et al.*, 2010).



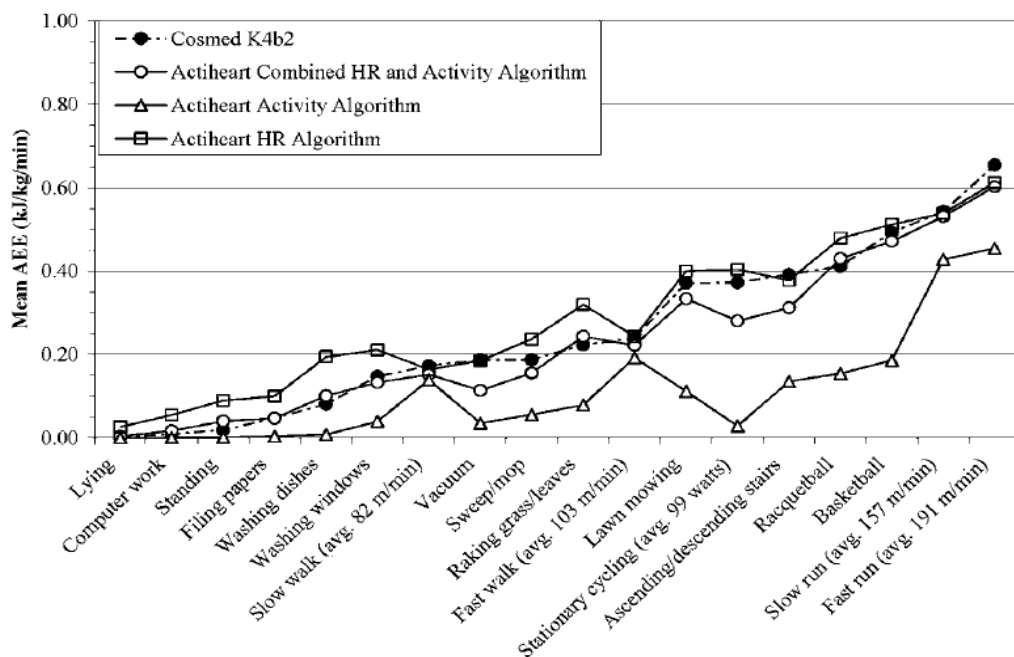
**Figure 1-6:** Linear regression between  $VO_2$  and HR during exercise workloads (Gastinger *et al.*, 2010).

### **1.1.7 Estimation of Body Energy Expenditure from Combined Heart Rate and Accelerometer Monitoring**

A number of studies have examined combining heart rate and motion sensor data to obtain improved estimates of BEE over the past several decades (Brage *et al.*, 2005; Zakeri *et al.*, 2008). Moon and Butte (1996) reported improved oxygen consumption predictions when heart rate and motion sensor data were combined. Similarly, Eston *et al.* (1998) demonstrated that a multiple regression equation which incorporated both triaxial accelerometry activity counts and heart rate gave superior accuracy in predicting oxygen consumption during physical activities than either accelerometry or heart rate alone. More recently, Brage *et al.* (2004) reasoned that because the limitations imposed by heart rate or accelerometer monitoring were not interrelated, simultaneous monitoring of both could potentially provide superior estimates of BEE and physical activity intensity.

The study by Brage *et al.* (2004) demonstrated that combined heart rate and accelerometer activity counts provided more accurate estimates of BEE than estimates that were derived from either heart rate or accelerometer activity accounts alone. This finding prompted the development of the Actiheart system, the first single piece device which combines heart rate and triaxial accelerometer data for the purpose of estimating BEE (Brage *et al.*, 2005). Studies with the Actiheart system have confirmed the findings of (Brage *et al.*, 2004) that combined heart rate and accelerometer monitoring provides superior estimates of BEE and physical activity intensity compared to that provided by either heart rate or accelerometer monitoring alone (Barreira *et al.*, 2009; Brage *et al.*, 2005; Corder *et al.*, 2005).

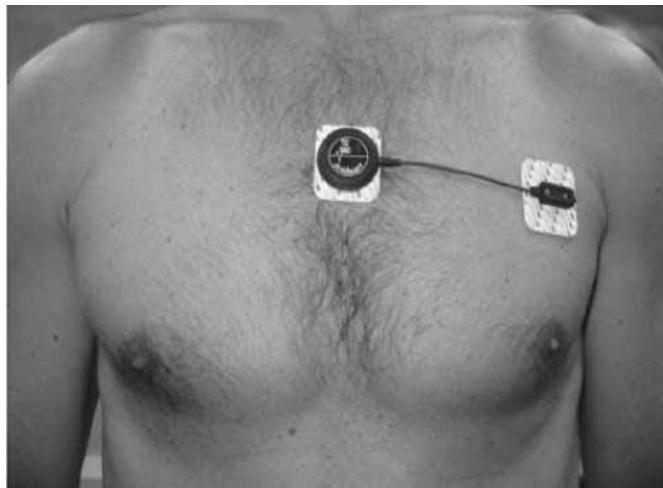
Several studies have demonstrated that the combined heart rate and accelerometer activity algorithm of the Actiheart system provides accurate estimates of energy expenditure during a diverse range of activities relevant to everyday life (Barreira *et al.*, 2009; Crouter *et al.*, 2008; Thompson *et al.*, 2006). This is illustrated in **Figure 1-7** from Crouter *et al.* (2008).



**Figure 1-7:** Activity energy expenditure (AEE) measured by indirect calorimetry with a Cosmed K4b<sup>2</sup> system and simultaneously estimated with an Actiheart system during 18 different daily activities (Crouter *et al.*, 2008).

The high accuracy during different activities under free living conditions, in combination with the small and unobtrusive nature of the Actiheart system, heralds new opportunities for the prolonged monitoring of BEE. Several diagrams help to illustrate this important point. **Figure 1-8** from Brage *et al.* (2005) demonstrates the small and unobtrusive nature of the Actiheart system when positioned on a person's chest. Telemetric indirect calorimetric systems such as the Jaeger Oxycon Mobile system can measure BEE under

remarkably unrestrained conditions as shown in *Figure 1-9*, but compared to the Actiheart system the equipment is bulky and requires a face mask which is unsuitable for prolonged measurements. In contrast, the Actiheart system can provide continuous accurate estimates of BEE over prolonged periods, as shown in *Figure 1-10* from Zakeri *et al.* (2008). In addition, it is significant to note that because of technical limitations little is known concerning the profile of daily BEE under free living conditions, but the Actiheart's ability to accurately and continuously estimate and digitally record BEE over prolonged periods of time (days or weeks) now provides a unique opportunity to address this deficiency.

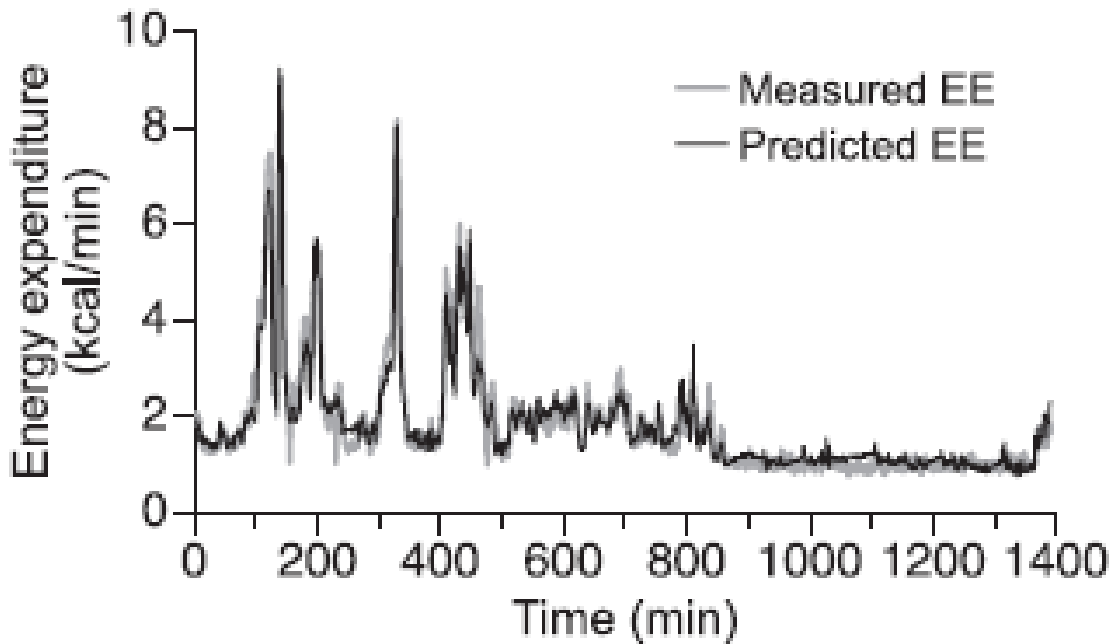


*Figure 1-8:* Actiheart system correctly placed on a participant to avoid vertical distortion in movement (Brage *et al.*, 2005).



**Figure 1-9:** The Jaeger Oxycon Mobile system which provides telemetric indirect calorimetric measurements of oxygen consumption (downloaded on 30<sup>th</sup> May, 2015 from [https://www.google.com.au/search?q=oxycon+mobile](https://www.google.com.au/search?q=oxycon+mobile&biw=1) and  $biw=1$ ).





**Figure 1-10:** Simultaneous room calorimeter measurements (measured EE) and Actiheart based estimates (predicted EE) of body energy expenditure during various activities throughout an entire 24 hour period (Zakeri *et al.*, 2008).

Earlier studies with the Actiheart system relied on the time consuming process of individually calibrating each participant's heart rate response to exercise (Brage *et al.*, 2004). However, Brage *et al.* (2007) subsequently demonstrated that group equations can be used with little loss in the accuracy of BEE estimates. In addition, as has been previously discussed (refer to *section 1.1.4*), the performance of many types of activity monitors is affected by where they are placed on the body. Therefore, Brage *et al.* (2006) examined the effect of body position on Actiheart performance and noted no difference in accuracy between Actiheart systems placed anteriorly over the left 3<sup>rd</sup> intercostal space and somewhat lower just under the apex of the sternum. Precise positioning of the Actiheart system is therefore not crucial for maintaining accuracy in BEE estimates.

Nichols *et al.* (2010) reported that the Actiheart system underestimated BEE during running in young female competitive runners, and that the error increased with increasing levels of exercise intensity. Barreira *et al.* (2009) also reported that the Actiheart system underestimated BEE somewhat during vigorous activities, but noted that this limitation did not detract from the usefulness of the Actiheart system because of the public health emphasis on low and moderate intensity activities.

Bassett *et al.* (2012) argued that greater attention needs to be given to validating activity monitors over the entire range of daily activities. Many of the studies which have validated the accuracy of the Actiheart system have concentrated on activities such as walking and running. However, such activities make only a minor contribution to the total daily BEE (Baptista *et al.*, 2012; Levine, 2004). In particular, little is known regarding the accuracy of Actiheart based estimates of BEE during common everyday daily activities that predominantly involve the arms and upper torso.

It is plausible that research into everyday daily activities that predominantly involve the arms and upper torso may uncover significant issues. As discussed previously (refer to *section 1.1.6*), the relationship between heart rate and oxygen consumption is affected by the type of exercise and body movements involved. This raises the question as to how effectively the Actiheart system's branched equation algorithms deal with the different heart rate responses to physical activities that involve different large muscle groups such as the legs versus the arms and upper torso.

The demonstrated accuracy of Actiheart based estimates of BEE during a wide range of daily activities that involve many different body movements and muscle groups (Barreira *et al.*, 2009; Crouter *et al.*, 2008; Thompson *et al.*, 2006) suggests that the Actiheart system is not adversely affected by different heart responses to different types of activities. However, a definitive answer to this question would require direct comparisons between the accuracy of Actiheart based estimates of BEE during equal intensities of arm and leg based exercise.

## 1.2 Clinical Application of Activity Monitoring

Investigations into the amount and intensity of physical activity necessary to promote and maintain health have in the past relied heavily on surveys and questionnaire based assessments. Such approaches continue to be widely used and information obtained in this way can be useful (Laporte *et al.*, 1985; Sallis and Saelens, 2000). However, data obtained in this manner is limited by subjective bias and the inability to accurately recall activities over a prolonged period. In addition, questionnaire based assessments cannot provide detailed moment-by-moment descriptions of the intensity and timing of activities over prolonged periods of time. Activity monitors have therefore been increasingly used over the past few decades to obtain more comprehensive information on people's patterns of physical activity. Indeed, the limitations posed by surveys and questionnaire based assessments of physical activity, coupled with growing concerns by health professionals about the modern sedentary lifestyle and the current obesity epidemic, have been a major impetus for the dramatic development of sophisticated activity monitors in recent years.

In addition to monitoring daily activity and BEE, activity monitors are nowadays also used to examine sleep patterns and circadian rhythms in various clinical disorders. Indeed, activity monitors are increasingly being used for diagnostic purposes and for evaluation of therapeutic outcomes in an increasingly diverse range of clinical conditions (Ancoli-Israel *et al.*, 2003).

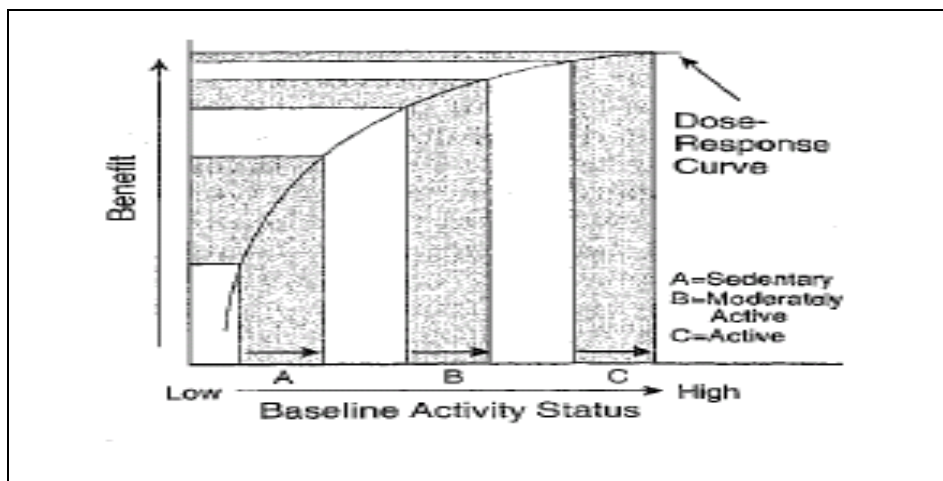
The type of activity monitor that is chosen is highly dependent on the type of data to be collected and the period of time over which measurements need to be made, and a wide range of different systems have been used in clinical settings. **Table 1-2** was compiled by the author and names some of the activity monitors used in clinical settings with references of validation studies.

**Table 1-2:** Activity monitors used in clinical settings.

<i>Type</i>	<i>Validation study</i>
<b>Accelerometers</b>	
<i>ActiGraph</i> (Inc., Baltimore,MD)	Vallieres and Morin (2003)
<i>RT3</i> (Stayhe althy, Inc., Monrovia, CA)	Hussey <i>et al.</i> (2009)
<i>Actical</i> (Philips Respironics)	Crouter <i>et al.</i> (2006)
<i>Actiwatch</i> (Philips Respironics)	Puyau <i>et al.</i> (2002)
<i>Actiwatch</i> (Cambridge Neurotech)	Ankers and Jones (2009)
<i>Biotrainer</i> (IM Systems)	Welk <i>et al.</i> (2003)
<i>Kenz Lifecorder</i> (Suzuken)	Yasunaga <i>et al.</i> (2008)
<i>Actitrac</i> (IM Systems, Baltimore, Md)	Strauss <i>et al.</i> (2001)
<i>Ikal</i> (Teltronic)	Berntsen <i>et al.</i> (2010)
<i>TriTrac</i> (Hemokinetics Inc., Madison WI)	Jacobi <i>et al.</i> (2007)
<i>Sleepwatch-O</i> (Ambulatory Monitoring)	Blackwell <i>et al.</i> (2008)
<i>Mini Motion Logger</i> (Ambulatory Monitoring)	Bisgaard <i>et al.</i> (1999)
<i>Gaehwiler</i> electronic Actimeter (Gaehwiler)	Hourmand-Ollivier <i>et al.</i> (2006)
<b>Multisensors</b>	
<i>Actiheart</i> (Cambridge Neurotech)	Brage <i>et al.</i> (2005)
<i>Caltrac</i> (Hemokinetics)	Calfas <i>et al.</i> (1996)
<i>ActiReg</i> (PreMed)	Hustvedt <i>et al.</i> (2004)
<i>IDEEA</i> (MiniSun)	Zhang <i>et al.</i> (2003)
<i>SenseWear Armband</i> (Body Media)	Berntsen <i>et al.</i> (2010)
<i>Sport Tester 3000</i> (Cranlea Medical)	Armstrong and Bray (1991)
<i>WatchPAT</i> (Itmar Medical)	Choi <i>et al.</i> (2010)
<b>Pedometers</b>	
<i>New Lifestyles</i> (New Lifestyles)	Crouter <i>et al.</i> (2003)
<i>Yamax Digiwalker</i> ( Yama)	Crouter <i>et al.</i> (2003)

### 1.2.1 Adverse Health Outcomes Resulting from Sedentary Lifestyle

There is a clear relationship between physical activity and health (Blair *et al.*, 2001; Pate *et al.*, 1995; Powell *et al.*, 1987). This relationship is schematically depicted in **Figure 1-11** from (Pate *et al.*, 1995). Similarly, there is a clear relationship between physical activity and reduced mortality (Andersen *et al.*, 2000; Blair *et al.*, 2001).



**Figure 1-11:** The base line activity status and health benefit dose response curve (Pate *et al.*, 1995).

Regular physical activity plays an important role in the prevention or amelioration of many chronic diseases (Haskell *et al.*, 2007). Increased physical activity is associated with a range of improved health outcomes, including in hypertension (Urata *et al.*, 1987), cardiovascular disease (Hu *et al.*, 2004; Lee *et al.*, 2001; Manson *et al.*, 2002; Sesso *et al.*, 2000; Smith *et al.*, 2000; Tanasescu *et al.*, 2002), diabetes mellitus (Lynch *et al.*, 1996), colon cancer (Colditz *et al.*, 1997) and to reduce the risk of overall mortality (Hu *et al.*, 2004; Lee and Skerrett, 2001; Paffenbarger *et al.*, 1993; Smith *et al.*, 2000; Warburton *et al.*, 2006).

Cooper *et al.* (1988) reported that increased physical activity, including increased activity within the house such as standing and walking, resulted in a reduced risk of hip fracture in elderly people. Ernst and Matrai (1987) noted improvements in blood viscosity and the maximum pain-free walking distance in patients with claudication after two months of regular exercise, and suggested that physical activity can assist in the treatment of peripheral arterial disease. In addition, many general population studies have reported that individuals who engaged in moderate and vigorous exercise had significantly lower mortality than those with low level of activity (Hu *et al.*, 2004; Lee and Paffenbarger, 2000; Lee and Skerrett, 2001; Paffenbarger *et al.*, 1993; Smith *et al.*, 2000; Warburton *et al.*, 2006). Of interest, factors other than reduced physical activity also contribute to increased mortality, including sedentary behavior. Patel *et al.* (2010) reported that the amount of time spent sitting was independently associated with increased risk of mortality, irrespective of the level of physical activity.

The protective effect of regular exercise on cardiovascular disease has been especially well studied for many years. In their extensive review, Powell *et al.* (1987) noted that the relative risk of developing coronary heart disease from physical inactivity was similar to the risk from hypertension, cholesterol or smoking. These findings confirm earlier reports that individuals with occupations with higher rates of physical activity had significantly reduced rates of coronary heart disease and mortality from coronary heart disease compared to those with sedentary occupations (Fox and Haskell, 1968; Morris and Crawford, 1958).

Modest weight loss can be achieved by increased physical activity (U.S. Department of Health, 2008). This is significant because increased body mass index (BMI) and obesity are themselves associated with a range of chronic disorders and adverse health outcomes, including hypertension, cardiovascular disease and type 2 diabetes (Ali and Crowther, 2005; Hu *et al.*, 2004; Kopelman, 2007; Wellman and Friedberg, 2002). Obesity is also an important risk factor for OSA and many OSA patients are overweight (Ali and Crowther, 2005; Young *et al.*, 2005; Young *et al.*, 1993).

Physical activity needs to be carried out with sufficient workload intensity and frequency for health benefits to occur (Haskell *et al.*, 2007; Lee and Paffenbarger, 2000). The American College of Sports Medicine, the American Heart Association and the Centers for Disease Control and Prevention have recommended that healthy adults need to undertake at least 30 minutes of moderately intense aerobic physical activity five days each week, or vigorous intensity physical activity for at least 20 minutes three days each week (Haskell *et al.*, 2007; Pate *et al.*, 1995). These reports also attempted to define physical activity and what constitutes low, moderate and vigorous physical activity (Haskell *et al.*, 2007; Pate *et al.*, 1995). Extensive compendiums of physical activities have been developed to facilitate



catagorising physical activities into different levels of intensity (Ainsworth *et al.*, 2000). In addition, (Baecke *et al.*, 1982) identified three components to physical activity which are necessary to understand the nature of the physical activity undertaken by an individual, physical activity at work, sport during leisure time and physical activity during leisure time other than sport.

Health benefits are evident even with moderate levels of regular physical activity. Warburton *et al.* (2006) argued that an increase in energy expenditure of  $4,200 \text{ kJ}\cdot\text{week}^{-1}$  is associated with a 20-30% decrease in mortality from all causes, although the intensity of the physical activities plays an important role. The (American College of Sports Medicine, 2011) position stand on the quantity and quality of exercise for maintaining health concluded that an increase in weekly energy expenditure of  $4,200 \text{ kJ}\cdot\text{week}^{-1}$  is associated with reduced rates of cardiovascular disease and premature mortality if the physical activities are sufficiently intense to raise the total energy expenditure to 3-5.9 times the resting metabolic rate. This position stand article further argued that reduced risks occur with increases in BEE of as low as  $2,100 \text{ kJ}\cdot\text{week}^{-1}$ .

### 1.2.1.1 Factors Impacting on Levels of Regular Physical Activity

The health benefits from regular physical activity underscore the importance of factors that influence how much physical activity a person will regularly undertake. However, levels of physical activity have been progressively falling for many years (Brownson *et al.*, 2005; Haskell *et al.*, 2007). Attitudes and approaches to physical activity are important in understanding the failure of individuals to maintain the recommended level of physical activity. Many factors, including demographic, physical environmental, psychological, socioeconomic and cultural, and environmental factors play significant roles in determining the level of physical activity undertaken (Brownson *et al.*, 2005; Trost *et al.*, 2002; Yasunaga *et al.*, 2008). Specific factors which have contributed to the reduced amount of physical activity engaged in include the increasing use of the motor vehicle as the primary mode of transport and reduced levels of occupational physical activity (Brownson *et al.*, 2005).

The extent of inadequate levels of physical activity in affluent countries is considerable. Haskell *et al.* (2007) reported that less than half (49.1 %) of adults in the USA engaged in recommended levels of physical activity. The challenges for reversing this trend are considerable. Low levels of habitual physical activity are already evident in children (Armstrong *et al.*, 1990), and there is concern that this and other unhealthy lifestyle behaviours may track from childhood to adulthood (Kelder *et al.*, 1994).

The prevalent adverse health outcomes resulting from inadequate physical activity provides a compelling reason to use activity monitors to accurately and unobtrusively monitor daily activities over prolonged periods under free living conditions. Activity monitors can provide useful feedback during intervention strategies aimed at promoting physical activity (Calfas *et al.*, 1996). Activity monitors may also play a useful role in promoting increased participation in physical activity, although there is the potential that inaccurate monitor data may provide an inflated measure of physical activity. In an interesting study with women who wished to increase their physical activity, Consolvo *et al.* (2006) noted improvements in physical activity due to feedback from pedometers which motivated participants to meet their physical activity targets.

### **1.2.2 Clinical Conditions with Impaired Mobility**

Adverse health outcomes occur irrespective of whether inadequate levels of physical activity are due to sedentary lifestyle choices or impaired physical mobility. Consequently, understanding physical activity levels is useful for optimising clinical outcomes in patients with mobility restrictions, as is found in nursing homes and residential care facilities, or in individuals who are restricted to the house through illness.

The importance of developing strategies that reduce physical decline during ageing is increasingly being recognised as populations are expected to age dramatically over the next few decades, but this will require a more detailed understanding of age related frailty (Rikli, 2000). Such concerns have prompted the use of activity monitors such as accelerometers to examine the daily activities of older adults and the elderly (Davis and Fox, 2007; Tudor-Locke *et al.*, 2002; Yasunaga *et al.*, 2008). In what appears to be the largest study of its kind

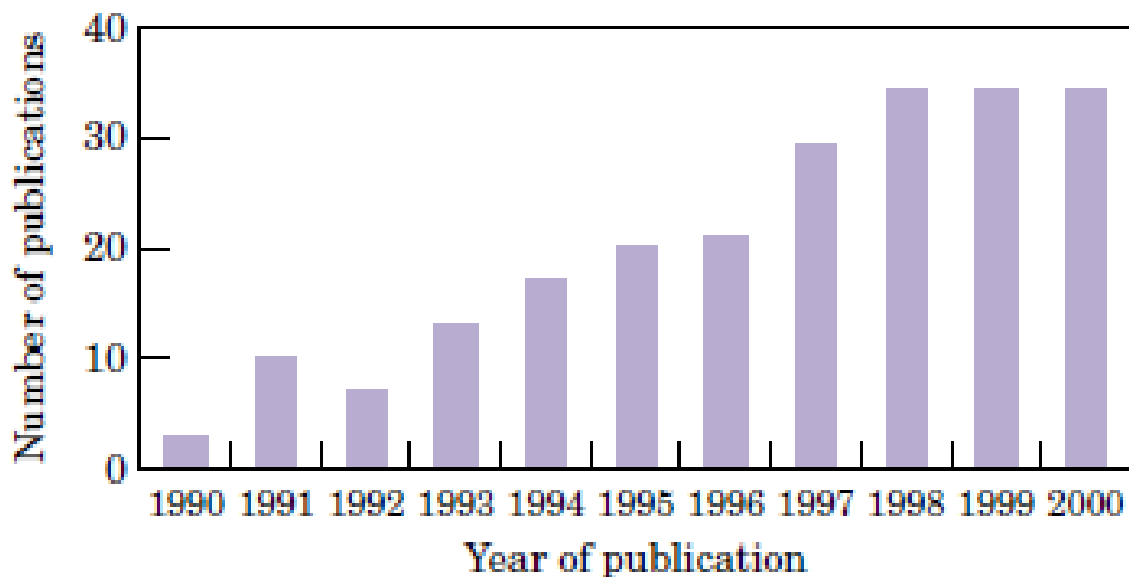
to date, Davis and Fox (2007) used accelerometers to quantify the decline in physical activity in a large group of 161 elderly men and women and noted that such information could help identify the extent to which the elderly meet their recommended activity dose requirements. Accelerometers and pedometers have also attracted interest as a means of better evaluating mobility and physical activity behaviours in other conditions, including overweight to severely obese individuals (Jacobi *et al.*, 2007; Papazoglou *et al.*, 2006), multiple sclerosis (Hale *et al.*, 2007; Motl *et al.*, 2005) and leg amputees (Dudek *et al.*, 2008).

Pitta *et al.* (2006) reviewed the literature and concluded that motion sensors provided more accurate information about physical activity in the daily life of patients with chronic obstructive pulmonary disease (COPD) than did questionnaires. In a previous study with accelerometers, (Pitta *et al.*, 2005) demonstrated that COPD patients were markedly inactive compared to age and gender matched control participants. Steele *et al.* (2000) reported that a triaxial accelerometer provided reliable and valid measurements of daily physical activity in COPD patients. Schonhofer *et al.* (1997) used pedometers to study daily activity in COPD patients and found that the step counts recorded by the pedometer per day correlated significantly with the forced expiratory volume in one second. However, pedometers did not detect increased activity in a group of patients with severe COPD following a program of pulmonary rehabilitation, even though improvements in dyspnoea, quality of life and exercise tolerance were noted (Dallas *et al.*, 2009). There is therefore a growing body of evidence that supports the use of activity monitors to evaluate impaired mobility in a range of clinical conditions.

### 1.2.3 Clinical Conditions with Disturbed Sleep and Abnormal Circadian Rhythms

Accelerometers have internal clocks which time stamp the digitised physical activity counts (Berlin *et al.*, 2006). This enables these devices to measure not only the intensity of activity, but also its timing, including the frequency, pattern and duration (Berlin *et al.*, 2006; Butte *et al.*, 2012; Freedson and Miller, 2000). These features make accelerometers especially well suited for monitoring sleep-wake patterns and circadian rhythms (Littner *et al.*, 2003). Consequently, actigraphy is increasingly being used in a diverse range of clinical conditions which are associated with sleep disorders and circadian rhythm abnormalities (Ancoli-Israel *et al.*, 2003; Tahmasian *et al.*, 2010). Indeed, as shown in **Figure 1-13**, Sadeh and Acebo (2002) reported a dramatic increase in the number of publications focusing on actigraphy and sleep in the decade from 1990 to 2000. Furthermore, the American Academy of Sleep Medicine has published recommendations to guide the clinical use of actigraphy (Littner *et al.*, 2003).

Wrist worn accelerometers appear to be especially suitable for monitoring sleep-wake patterns and circadian rhythms in patients with sleep disorders. Data obtained from wrist worn accelerometers has been shown to be comparable with that obtained from polysomnography in patients with sleep disorders, especially when the actigraphic data is used in conjunction with subjective sleep assessment questionnaires (Kushida *et al.*, 2001; Lötjönen *et al.*, 2003).



**Figure 1-12:** Number of yearly publications focusing on actigraphy and sleep (Sadeh and Acebo, 2002).

Actigraphic studies have been reported in patients with sleep disorders associated with a diverse range of clinical conditions including, delayed sleep phase syndrome (Nagtegaal *et al.*, 1998), periodic limb movement disorder of sleep in children (Crabtree *et al.*, 2003) and adults (Allen *et al.*, 2003), sleep impairment in the elderly (Youngstedt *et al.*, 2001), convalescence after major abdominal surgery (Bisgaard *et al.*, 1999) and insomnia associated with chronic musculoskeletal pain (Wilson *et al.*, 1998). In addition, actigraphic monitoring of sleep-wake patterns and circadian rhythms has proven useful in a range of other clinical conditions, including cancer, psychiatric conditions, and sleep disordered breathing conditions such as obstructive sleep apnoea (OSA).

### 1.2.3.1 Cancer

Sleep disturbances are a frequent concern in patients with cancer, and psychometric scoring of sleep with questionnaires in these patients is cumbersome (Beck *et al.*, 2004). The ability of accelerometers to provide information on daily sleep patterns has therefore proven invaluable in patients with cancer. Berger *et al.* (2008) reviewed 21 studies that used actigraphy to assess sleep and wakefulness in cancer patients.

A number of studies have examined the utility of wrist worn actigraphs to evaluate sleep patterns and circadian rhythms in cancer patients (Ancoli-Israel *et al.*, 2006; Berger *et al.*, 2007; Chevalier *et al.*, 2003; Du-Quiton *et al.*, 2010; Mormont *et al.*, 2000). Ancoli-Israel *et al.* (2006) used wrist worn accelerometers to examine sleep patterns and circadian rhythms in breast cancer patients and noted sleep disturbances and fatigue before the patients commenced chemotherapy. Using wrist worn accelerometers, Chevalier *et al.* (2003) noted that the large difference in activity between daytime and nocturnal sleep evident in normal healthy participants was less apparent in patients with advanced colorectal cancer. Du-Quiton *et al.* (2010) used wrist worn accelerometers in lung cancer patients and demonstrated that daily sleep-activity cycles were extremely disturbed, and that the severity of the disturbed sleep-activity cycles in outpatients correlated with the severity of anxiety and depression. Mormont *et al.* (2000) used wrist worn accelerometers to determine the rest/activity circadian cycle in cancer patients in order to deliver chronomodulated chemotherapy with improved tolerance and efficacy. Of interest, these investigators reported that patients with less rest time and more time while active had improved quality of life and significantly improved survival time compared to patients who had a less pronounced rest/activity circadian cycle.

### 1.2.3.2 Psychiatric Conditions

Actigraphic evaluation of sleep-wake patterns and activity levels has been used to investigate, diagnose, and to evaluate therapeutic outcomes, in a range of psychiatric disorders, including bipolar disorder (Ankers and Jones, 2009; Cole *et al.*, 1992; Jones *et al.*, 2005; Wirz-Justice *et al.*, 1999), dementia (Ancoli-Israel *et al.*, 1997; Pat-Horenczyk *et al.*, 1998) and schizophrenia (Dursun *et al.*, 1999; Haug *et al.*, 2000; Martin *et al.*, 2001).

Actigraphy is regarded as highly suitable for studying sleep and awake activity in dementia patients (Ancoli-Israel *et al.*, 1997). This is because diffuse slowing of the waking electroencephalogram limits the ability of conventional electroencephalographic techniques to detect the complete fragmentation of sleep and wakefulness states which occurs in severe dementia (Pat-Horenczyk *et al.*, 1998). Actigraphic studies have also revealed significantly disturbed sleep patterns and circadian rhythms in patients with schizophrenia (Dursun *et al.*, 1999; Martin *et al.*, 2001) and bipolar disorder (Ankers and Jones, 2009; Jones *et al.*, 2005). Moreover, the circadian rhythm disruptions were evident before manifestation of bipolar symptoms, suggesting that actigraphic information may be useful for early intervention (Ankers and Jones, 2009; Jones *et al.*, 2005).



### 1.2.3.3 Sleep Disordered Breathing

There has been considerable interest in identifying and validating cheaper and more convenient alternatives for diagnosing OSA (Ahmed *et al.*, 2007; Berry *et al.*, 2008). One potential alternative that has been explored for this purpose is actigraphy (Ancoli-Israel *et al.*, 2003; Berry *et al.*, 2008; García-Díaz *et al.*, 2007). Such investigations have utilised actigraphy in combination with self-report questionnaires or sleep logs (Kushida *et al.*, 2001; Middelkoop *et al.*, 1995) and other biological sensors (Berry *et al.*, 2008; García-Díaz *et al.*, 2007). The results of these investigations have often been encouraging (García-Díaz *et al.*, 2007; Kushida *et al.*, 2001), although contrary findings have also been reported (Middelkoop *et al.*, 1995).

Although various studies have reported actigraphic monitoring of sleep disturbances and circadian rhythm abnormalities in OSA, very little is known about objective measures of daily activities such as daily BEE in OSA. This is surprising given that subjective questionnaire derived data indicate that OSA patients are less active than healthy individuals (Chasens *et al.*, 2011), and OSA patients frequently display excessive daytime sleepiness (Malhotra and White, 2002; Remmers *et al.*, 1978) which can be reversed by continuous positive airway pressure (CPAP) therapy (McArdle and Douglas, 2001; Montserrat *et al.*, 2001; Patel *et al.*, 2003). These findings suggest that reduced daily activity in OSA patients is due to excessive daytime sleepiness, and that this could be reversed by nightly CPAP therapy. However, this possibility does not appear to have been investigated, and such a study would ideally involve objective quantification of daily activities such as measurements of daily body energy expenditure.

### 1.3 Obstructive Sleep Apnoea

OSA is a common and serious clinical condition that occurs as a result of repeated episodes of pharyngeal airway obstruction during sleep which leads to repeated apnoeas and hypopnoeas with resultant sleep fragmentation and frequent arousals from sleep, and excessive daytime sleepiness (Eckert and Malhotra, 2008; Guilleminault *et al.*, 1976; Hudgel, 1992; McNicholas and Ryan, 2006; Victor, 1999).

OSA is a common and frequently underdiagnosed condition (Young *et al.*, 2002). The prevalence of OSA has been estimated to be 1 to 5% in adults (Young *et al.*, 2002). Substantial differences in OSA prevalence have been reported in different populations, and this may at least in part reflect racial differences (Stradling and Davies, 2004). However, it is significant to note that calculation of reliable estimates of OSA prevalence has been hampered by the lack of a clear and unambiguous definition of OSA, and that prevalence of OSA is consequently heavily dependent on the number of hourly apneas and hypopnoeas during sleep that are used to identify whether clinically significant OSA is present (Stradling and Davies, 2004).

### 1.3.1 Pathophysiology of OSA

The principal sites of airway obstruction in OSA are the nasopharynx and oropharynx, although the hypopharynx can also be involved (Chaban *et al.*, 1988; Hudgel and Hendricks, 1988; Rojewski *et al.*, 1982; Shepard and Thawley, 1990; Suratt *et al.*, 1983). The pharynx is a collapsible tube and its patency is determined by the net balance between the forces acting to collapse it and the forces resisting such collapse (Block *et al.*, 1984; Hudgel, 1992; Malhotra and White, 2002). Negative (subatmospheric) pharyngeal airway pressure generated during inspiration acts to suck in and collapse the pharynx (Block *et al.*, 1984; Malhotra and White, 2002). A major force acting to prevent collapse is generated by various pharyngeal skeletal dilator muscles such as the genioglossus muscle of the tongue, but the activity of these muscles is diminished during sleep (Block *et al.*, 1984; Hudgel, 1992; Malhotra and White, 2002).

Remmers *et al.* (1978) noted increased genioglossal electromyographic activity when the collapsed pharynx opened during arousal in sleeping OSA patients, and argued that the genioglossal contraction provided an important dilator action. Hypoxaemia and hypercapnia from apnoeas/hypopnoeas are believed to be involved in evoking the transient arousals from sleep (Malhotra and White, 2002). Although the existence of a direct causal relationship between arousals and apnoea termination has been challenged (Younes, 2004), apnoea termination and arousal are usually closely linked temporally (Eckert and Malhotra, 2008; Younes, 2004), and patients with untreated OSA often experience hundreds of apnoeas/hypopnoeas during a night's sleep (Eckert and Malhotra, 2008; Victor, 1999). The sleep fragmentation is believed to be responsible for the excessive daytime sleepiness which

is typically present in patients with significant OSA (Malhotra and White, 2002; Victor, 1999).

### 1.3.2 Comorbidities Associated with OSA

Many patients with OSA are overweight or obese and middle aged to older individuals, and are therefore at increased risk of developing clinical conditions such as cardiovascular disease and diabetes. The extent to which OSA is itself an independent risk factor for such clinical disorders has been therefore been debated (Wright *et al.*, 1997), and this has led to further research into these issues with properly controlled studies (Davies and Stradling, 2000; Park *et al.*, 2011). Many studies have reported that OSA is a risk factor for a range of chronic disorders and adverse health outcomes, including hypertension (Akahoshi *et al.*, 2010; Nieto *et al.*, 2000; Parish and Shepard, 1990; Peppard *et al.*, 2000; Silverberg *et al.*, 2002), cardiovascular disease (Marin *et al.*, 2005), glucose intolerance, insulin resistance and type 2 diabetes (Akahoshi *et al.*, 2010; Punjabi *et al.*, 2004; West *et al.*, 2006) and death from cardiovascular events (Marin *et al.*, 2005; Parish and Shepard, 1990). Importantly, many studies have reported that these adverse health outcomes improve after commencement of nightly CPAP therapy (Doherty *et al.*, 2005; Harsch *et al.*, 2004; Marin *et al.*, 2005; Parish and Shepard, 1990; Silverberg *et al.*, 2002), which strengthens the case that OSA is itself an independent risk factor for these comorbidities. However, the mechanism/s responsible for these improvements remains unclear (Akahoshi *et al.*, 2010; Mohan and Kumar, 2013).

### 1.3.3 Treatment Options for OSA

A diverse range of therapeutic options which attempt to favourably shift the balance of forces acting on the pharynx to promote pharyngeal patency have been explored as potential therapies for the clinical management of OSA. In addition to nightly CPAP therapy (D'Ambrosio *et al.*, 1999; Davies and Stradling, 2000; Montserrat *et al.*, 2001; Sullivan *et al.*, 1981), these include uvulopalatopharyngoplasty involving surgical resection of the soft palate and pharyngeal wall (Ringqvist *et al.*, 2003; Shepard and Thawley, 1989), promoting protrusion of the tongue by maxillofacial surgery involving maxillomandibular advancement (Conradt *et al.*, 1997; Prinsell, 1999; Riley *et al.*, 1990) or insertion of mandibular advancement dental devices before sleep (Ringqvist *et al.*, 2003), pharmacological treatment to stimulate ventilatory drive, increase upper airway muscle tone and decrease REM sleep (Hudgel and Thanakitcharu, 1998; Issa, 1992), submental electrical stimulation of the genioglossus muscle (Miki *et al.*, 1989) and electrical atrial overdrive pacing to stabilize respiration (Unterberg *et al.*, 2005).

Some therapies other than CPAP can be of benefit in a limited selection of OSA cases. However, CPAP therapy is the treatment of choice for patients with moderate to severe OSA (Engleman *et al.*, 1994; Epstein *et al.*, 2009; Grunstein and Sullivan, 2000; Marrone *et al.*, 2002; Mcardle *et al.*, 1999; Park *et al.*, 2011; Strollo and Rogers, 1996).

### 1.3.4 CPAP Therapy

Prior to the advent of CPAP therapy it was known that sleep fragmentation and excessive daytime sleepiness in OSA patients could be reversed by tracheostomy or tracheal intubation to bypass the upper airway (Guilleminault *et al.*, 1976). Consequently, Sullivan *et al.* (1981) was the first to use positive air pressure applied continuously to the pharynx via the nares (i.e. nasal CPAP) as a therapy for OSA to pneumatically splint open the pharyngeal airways during sleep.

Many reports have noted positive effects and improved health outcomes after commencement of nightly CPAP therapy in OSA patients. These effects include reductions in arousals (Loredo *et al.*, 1999; Loredo *et al.*, 2006) and arterial desaturation (Loredo *et al.*, 1999; Loredo *et al.*, 2006), as well as improvements in the respiratory disturbance index (Loredo *et al.*, 1999; Loredo *et al.*, 2006), sleep fragmentation (D'Ambrosio *et al.*, 1999; Grunstein and Sullivan, 2000), sleepiness (Jenkinson *et al.*, 1999; McArdle and Douglas, 2001; Montserrat *et al.*, 2001; Patel *et al.*, 2003) and functional outcomes, quality of life and self-reported health outcomes (D'Ambrosio *et al.*, 1999; Jenkinson *et al.*, 1999; Montserrat *et al.*, 2001). However, in their critical review of the literature, Wright *et al.* (1997) argued that, with the possible exception of reduced daytime sleepiness, there was insufficient evidence from properly controlled studies to justify these claims. The report by Wright *et al.* (1997) stimulated considerable further research which confirmed the health benefits from CPAP therapy in patients with moderate and severe OSA “*beyond any reasonable doubt*” (Davies and Stradling, 2000). Whether this also applies in patients with mild OSA is however less clear (Barnes *et al.*, 2002; Davies and Stradling, 2000; Engleman *et al.*, 1999; Engleman *et al.*, 1997; Wright and Sheldon, 2000).

Although CPAP is effective in the treatment of OSA, there are significant side effects and limitations. Many OSA patients receiving CPAP therapy complain of side effects such as nasal problems and nocturnal awakenings (Engleman *et al.*, 1994; Hoffstein *et al.*, 1992; Rueda *et al.*, 2009; Sanders *et al.*, 1986). Patient noncompliance is also an issue, with a significant number of OSA patients abandoning nightly CPAP therapy or only using CPAP intermittently (Engleman *et al.*, 1994; Hoffstein *et al.*, 1992; Rueda *et al.*, 2009; Sanders *et al.*, 1986). Side effects from CPAP contribute to noncompliance. Engleman *et al.* (1994) noted that OSA patients who reported side effects from CPAP were less inclined to use CPAP and emphasised the importance of good clinical follow up to minimize such complications. In addition, Rueda *et al.* (2009) reported that a basic and inexpensive educational program improved CPAP compliance.

## **1.4 Actigraphic Evaluation of Daily Activities and Body Energy**

### **Expenditure in OSA**

Data from subjective self-reporting questionnaires suggest that OSA patients are less active than healthy individuals (Chasens *et al.*, 2011). This is not surprising given that OSA patients frequently display excessive daytime sleepiness (Malhotra and White, 2002; Remmers *et al.*, 1978). The study by Chasens *et al.* (2011) used the Functional Outcomes of Sleep Questionnaire to assess different activities of daily living, but these data do not translate into quantifiable levels of physical activity. In addition, questionnaire based data relating to daily activities is limited by subjective bias and the inability to accurately recall activities over a prolonged period. Furthermore, very little is known about objective measures of daily activities such as daily body energy BEE expenditure in OSA.

Recent advances in actigraphy allow accurate estimates of BEE to be made in an unobtrusive manner over prolonged periods of time. However, although actigraphy is increasingly being used to clinically monitor sleep disturbances and circadian rhythm abnormalities in OSA, the author is aware of only one study that has used actigraphic techniques to make day long objective measurements of daily activities and BEE in patients with OSA (Chasens *et al.*, 2011). These investigators used a two-axial accelerometer Bodymedia Armband to objectively measure body energy expenditure, but failed to find a correlation between the objective measurements of daily activity from this device and the subjective self-reporting scores of daily activity. However, it should be noted that a number of studies have reported poor accuracy with Bodymedia Armband based energy expenditure estimates when compared against simultaneous indirect calorimetric measurements in normal and obese participants at rest and during a range of physical activities (Berntsen *et al.*, 2010; Bertoli *et al.*, 2008; Papazoglou *et al.*, 2006; Soric *et al.*, 2012).

Excessive daytime sleepiness can be reversed by continuous positive airway pressure (CPAP) therapy (Jenkinson *et al.*, 1999; McArdle and Douglas, 2001; Montserrat *et al.*, 2001; Patel *et al.*, 2003). These findings suggest that if reduced daily activity in OSA patients is due to excessive daytime sleepiness, then this could be reversed by nightly CPAP therapy. This possibility does not appear to have been investigated and warrants investigation. Such a study would ideally involve objective quantification of daily activities such as measurements of daily body energy expenditure. The Actiheart system, which utilises triaxial accelerometry and heart rate data, would appear to be the best suited equipment currently available for this purpose as it has been well validated and shown to give reliable and accurate estimates of BEE in an unobtrusive manner over prolonged periods during a diverse range of activities relevant to everyday life (Barreira *et al.*, 2009; Crouter *et al.*, 2008; Thompson *et al.*, 2006).



Until recently, technical limitations have prevented making prolonged measurements of BEE under free living conditions. Consequently, very little is known concerning the profile of daily BEE and how this is influenced by disease. However, the Actiheart's ability to accurately and continuously estimate and digitally record BEE over prolonged periods of time (days or weeks) now provides a unique opportunity to address this deficiency.

An enhanced ability to accurately monitor daily activities and BEE in OSA patients has potentially significant clinical implications. Increased physical activity is associated with a range of improved health outcomes, including reduced hypertension (Urata *et al.*, 1987), cardiovascular disease (Hu *et al.*, 2004; Lee *et al.*, 2001; Manson *et al.*, 2002; Sesso *et al.*, 2000; Smith *et al.*, 2000; Tanasescu *et al.*, 2002), diabetes mellitus (Lynch *et al.*, 1996) and mortality (Hu *et al.*, 2004; Lee and Skerrett, 2001; Paffenbarger *et al.*, 1993; Smith *et al.*, 2000; Warburton *et al.*, 2006). As has already been discussed, these adverse health outcomes commonly afflict OSA patients. This raises the question as to whether a CPAP related increase in daily activities could induce improved health outcomes in patients with OSA.

In view of the issues covered in this review of the literature, the author conducted a series of investigations to evaluate the accuracy of Actiheart based estimates of BEE, examine daily BEE in patients with OSA and how BEE varied throughout the day, and determine whether daily BEE and the daily BEE profile in OSA patients changed after commencement of nightly CPAP therapy.

## Chapter 2 Evaluating the Accuracy of Actiheart Derived Estimates of Body Energy Expenditure

### 2.1 Introduction

In recent years, technological advances have made it possible to obtain accurate long-term estimates of BEE using small portable devices that can be worn. The available literature suggests that the Actiheart system (CamNtech Neurotechnology Ltd, Cambridge UK) is superior for this purpose because it incorporates Electrocardiogram (ECG) based heart rate data plus motion sensor data from accelerometers to derive accurate estimates of BEE (Brage *et al.*, 2005; Corder *et al.*, 2005).

Although Actiheart systems have been available since 2005, a few studies have already demonstrated that the Actiheart provides accurate estimates of BEE (Brage *et al.*, 2007; Crouter *et al.*, 2008; Thompson *et al.*, 2006; Zakeri *et al.*, 2008). However, although the Actiheart system is a relatively new device, several versions have already been released commercially (Crouter *et al.*, 2008). This necessitates evaluation of the accuracy of newly acquired Actiheart systems in our laboratory. In addition, it remains unclear whether the accuracy of BEE estimates is substantially diminished if the time consuming process of calibrating each experimental participant with graded exercise workloads is replaced with group based equations such as those published by Brage *et al.* (2007).

For these reasons, a study was conducted to determine the accuracy of the Actiheart derived BEE estimates using the group based equations by Brage *et al.* (2007) under a range of resting and exercise treadmill conditions in healthy participants.

### 2.1.1 Aim of the Study

A pilot study was carried out to determine the accuracy of the Actiheart derived BEE estimates using the group based equations by Brage *et al.* (2007) in healthy participants under a range of resting and exercise treadmill conditions. In addition, it was considered necessary to examine whether the chest straps from the mobile telemetric Oxycon mobile system used to measure oxygen consumption interfered with the function of the Actiheart's accelerometers, and whether the telemetric Oxycon signals produced electrical interference with the Actiheart system.

## 2.2 Materials and Methods

Approval for the study was obtained from the Human Research Ethics Committee of the University of New England (Approval No. HE10/186, Valid to 05/11/2011). Each participant gave informed consent prior to commencement of the study. Each participant was carefully instructed that they could withdraw from the study at any time without penalty. Before being recruited into the study, each participant completed a basic PAR-Q physical activity readiness questionnaire (Physical Activity Readiness Questionnaire, 2002).

### 2.2.1 Participants

Six healthy men were recruited into this study. The participants were non-smokers, non-athletes and did not have any evidence of physical disability or current disease that would affect their exercise capacity. All were from the University of New England student population and were approached and invited by the author to participate in the study.

## 2.2.2 Equipment

### 2.2.2.1 Actiheart

An Actiheart system (Actiheart 4, AH4, CamNtech Neurotechnology Ltd, Cambridge UK) was used to indirectly estimate BEE using heart rate and body movement data. The Actiheart system was worn attached to the left side of the participant's anterior chest by means of 2 horizontally positioned ECG electrodes. Heart rate was recorded over 60 second epochs by the Actiheart system using the electrocardiographic R wave to R wave interval with a Pan Tompkins read time algorithm (Pan and Tompkins, 1985). One minute recording epochs were chosen to facilitate direct comparison between simultaneous one minute long Actiheart based estimates and indirect calorimetric measurements of energy expenditure. A data sampling rate of 128 Hz was used as specified by the manufacturer in the Actiheart user manual (CamNtech Neurotechnology Ltd, Cambridge UK, user manual. v 4.0.35, 2010).

### 2.2.2.2 Oxycon Mobile

Indirect calorimetric measurements of BEE were made by measuring Oxygen consumption ( $\dot{V}O_2$ ) using a portable telemetric Oxycon Mobile system (Oxycon Mobile® Erich Jaeger, Viasys Healthcare, Hochberg Germany). This portable and mobile cardiopulmonary exercise testing system continuously measured the expired air volumes, and the oxygen and carbon dioxide concentrations of inhaled and exhaled air to provide breath-by-breath measurements of  $\dot{V}O_2$ , rate of carbon dioxide production ( $\dot{V}CO_2$ ) and the respiratory exchange ratio ( $RER = \dot{V}CO_2 \div \dot{V}O_2$ ). The Oxycon Mobile system allows direct line-of-sight telemetric transmission of all measured cardiorespiratory parameters up to a distance of 500 meters.

The Oxycon Mobile system consisted of a power calibration unit, a sensor box, a data transfer/recording Unit, a flash card for data storage and transfer, a telemetric transmitter, a lithium-ion battery, an ear oximeter with lead and an adjustable face mask connected to a turbine volume sensor and an air sampling port. Items other than the face mask were attached to the participant's chest or back using a harness. *Figure 2-1* shows the author wearing the Oxycon Mobile system and holding the Actiheart system in his hand to contrast the relative size and bulkiness of these two pieces of equipment.



*Figure 2-1:* The author wearing the Oxycon Mobile system and holding the Actiheart system in his left hand. Note the difference in size and bulkiness of these two pieces of equipment.

### 2.2.3 Experimental Protocol

Participants were asked to refrain from eating or drinking (except water), smoking, vigorous exercise and any high intensity effort for at least 2 hour before arriving at the laboratory. The height of each participant measured to the nearest 0.5 cm with a standard stadiometer (without shoes). Body weight was measured to the nearest tenth of a kilogram in each participant wearing light clothing using a body composition monitor with scales (Omron Healthcare Co. Ltd, Japan, model HBF-500). Body mass index (BMI) was calculated for each participant as: Body mass (kg) divided by height squared ( $m^2$ ).

#### 2.2.3.1 Equipment Calibration and Participant Instrumentation

Two disposable ECG electrodes (Red Dot 2560, 3M/Canada) were used to obtain Actiheart heart rate measurements. The medial electrode was positioned at the level of the left 4<sup>th</sup> intercostal space just under the apex of the sternum (V1 or V2 pectoral lead position) and the lateral electrode was placed 12–13 cm horizontally to the left at the V4 or V5 pectoral lead position as recommended by Brage *et al.* (2005). Before positioning the ECG electrodes, the underlying skin was thoroughly cleansed and degreased with warm water and isopropyl alcohol swabs to optimise skin electrical conductivity and minimize electrical interference. Once the Actiheart was correctly positioned, the sleep heart rate was then estimated as instructed in the Actiheart user manual (CamNtech Neurotechnology Ltd, Cambridge UK, user manual. v 4.0.35, 2010).

The Oxycon Mobile system was allowed to warm up for at least 15 minutes prior to use as recommended by the manufacturer. A series of calibrations were then carried out prior to each study. First, air humidity, air temperature, and barometric pressure were measured with a whirling hydrometer and barometer, and these values were entered into the Oxycon software file on a dedicated personal computer as instructed by the manufacturer. In addition, respiratory volumes were calibrated with a 3 liter gas syringe (Hans Rudolph, inc Shawnee USA, series 5530) connected to the Oxycon's turbine volume sensor, and measurements of oxygen O<sub>2</sub> and carbon dioxide CO<sub>2</sub> air concentrations were calibrated by using known gas standards 17.00% O<sub>2</sub> and 6.00% CO<sub>2</sub> (BOC Gases, Australia Ltd). These calibrations were carried out in accordance with the manufacturers' instructions (Oxycon Mobile® Erich Jaeger, Viasys Healthcare, Hochberg Germany. user manual. v 5.2, 2007). All transducers, the telemetry system and the charged lithium battery were connected to a custom made vest which was worn on the back of the participant to ensure that there was no contact with the Actiheart system. An ear oximeter probe was connected to the left ear lobe to measure heart rate. The participant was then fitted with an appropriately sized face mask which was connected to the turbine volume sensor and an air sampling catheter. Care was taken to ensure that the face mask gave an airtight seal.

### **2.2.3.2 Rest and Exercise Protocol**

Once fully instrumented, each participant underwent the following rest and exercise protocol while data was simultaneously recorded by both the Actiheart and Oxycon Mobile systems: 1) three minutes of rest while sitting, 2) three minutes of rest standing quietly on a treadmill, 3) three minutes of treadmill walking at 3 km.hr<sup>-1</sup>, 4) three minutes of treadmill walking at 5 km.hr<sup>-1</sup> and 5) three minutes of treadmill walking at 7 km.hr<sup>-1</sup>. Treadmill walking

was carried out on a Cosmos treadmill (Wood Way® Waukesha, Wisconsin USA, model no pro XL) at zero inclination.

These intensities of treadmill exercise used in this study were classified as low (3 km.hr<sup>-1</sup>) and moderate (5 and 7 km.hr<sup>-1</sup>) in accordance with the published compendiums of physical activities (Ainsworth *et al.*, 1993; Ainsworth *et al.*, 2000; American College of Sports Medicine, 2011; Garber *et al.*, 2011; Haskell *et al.*, 2007). These resting and low to moderate levels of exercise intensity were chosen because they were likely to be most relevant to the normal daily behavior of patients with impaired physical capacity.

#### 2.2.4 Data Analysis

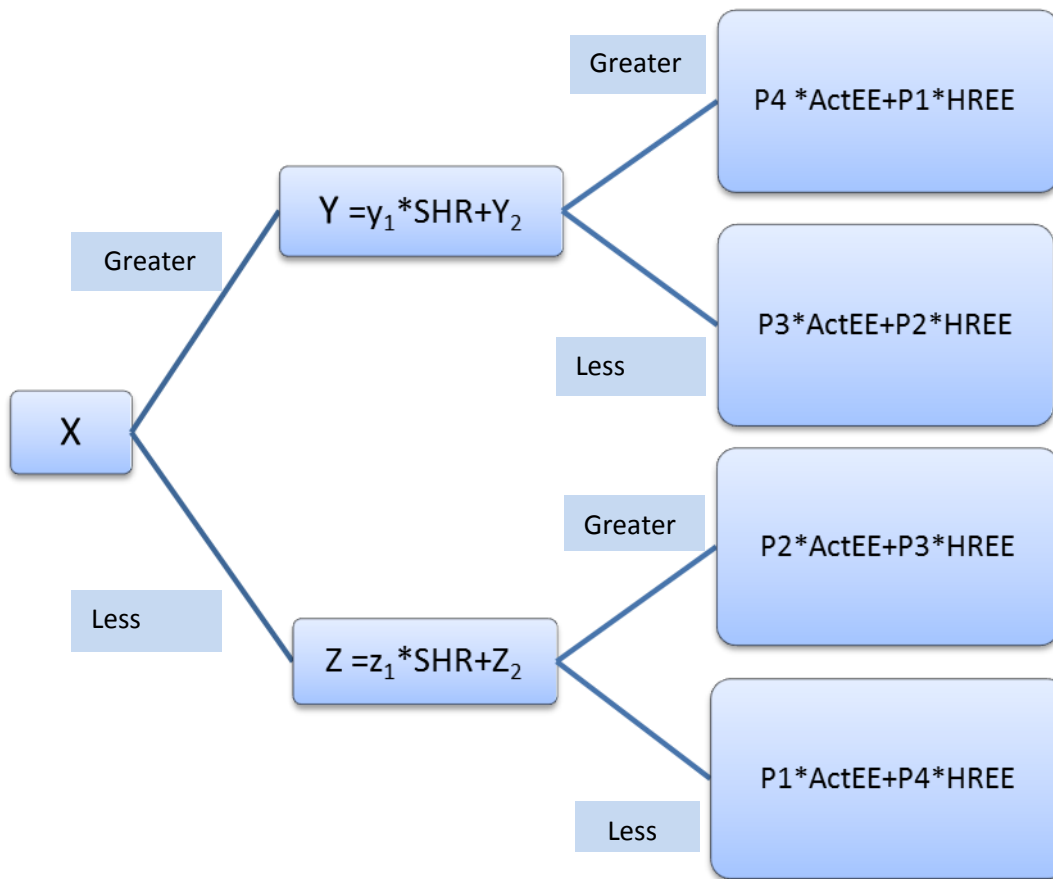
Heart rate and body movement data recorded with the Actiheart system were transferred onto a lap top computer using an Actiheart reader system (CamNtech Neurotechnology Ltd, Cambridge UK, serial no 320208). Actiheart system software (CamNtech Neurotechnology Ltd, Cambridge UK. software v.4.0.89) was used to analyse the recorded Actiheart data over 60 second epochs using a validated branched-equation model with the group based equation by Brage *et al.* (2007) (refer to **Figure 2-2**).



As shown in **Figure 2-2**, The Actiheart's calculating mode respectively switches to the Y or Z modes depending on whether the activity output  $\geq 25$  count per minute (cpm) or not. If the activity output  $\geq 25$  cpm and the participant's heart rate  $\geq$  the value calculated by the equation  $Y = (0.54 \times \text{SHR}) + 54.3$  bpm (i.e.  $y_1 \times \text{SHR} + y_2$ ), then the Actiheart's calculating mode calculates BEE as  $P4 \times \text{ActEE} + P1 \times \text{HREE}$ . In contrast, BEE is calculated as  $P3 \times \text{ActEE} + P2 \times \text{HREE}$  if the participant's heart rate was less than the value calculated by the equation  $Y = y_1 \times \text{SHR} + y_2$ . If the activity output  $< 25$  cpm and the participant's heart rate  $\geq$  the value calculated by the equation  $Z = (0.05 \times \text{SHR}) + 21.2$  bpm (i.e.  $z_1 \times \text{SHR} + z_2$ ), then the Actiheart's calculating mode calculates BEE as  $P2 \times \text{ActEE} + P3 \times \text{HREE}$ . In contrast, BEE was calculated as  $P1 \times \text{ActEE} + P4 \times \text{HREE}$  if the participant's heart rate was less than the value calculated by the equation  $Z = z_1 \times \text{SHR} + z_2$ .

The following Actiheart settings were used in this study: the advanced BEE tab was first selected, then the setup tab, the 1 minute long term recording option was then selected by the tab (send) to start recording, and BEE data was later read in  $\text{kJ} \cdot \text{min}^{-1}$ .

Data collected by the Oxycon Mobile system was transferred to a lap top computer and analysed using dedicated software (CardinalHealth, Hochberg, Germany. JLAB software v. 5.22.1). Oxygen consumption based measurements of BEE were calculated breath-by-breath for each minute's values of RER and  $\text{VO}_2$ , and the corrected BEE values were expressed in  $\text{kJ} \cdot \text{min}^{-1}$  (Fox and Mathews, 1981).



**Figure 2:2** flow chart modified from (Brage *et al.*, 2007) equation.

The flow chart depicts the branch-equation model used by the Actiheart system to estimate BEE under conditions of varying body activity. Note that X represents the electronic activity output in counts per minute (cpm) from the accelerometers, Y is a heart rate threshold in bpm,  $y_1 = 0.54$ ,  $y_2 = 54.3$  bpm, SHR is the participant's SHR or estimate thereof, Z is a heart rate threshold in bpm,  $z_1 = 0.05$ ,  $z_2 = 21.2$  bpm,  $P_1 = 0.9$ ,  $P_2 = 0.5$ ,  $P_3 = 0.5$ ,  $P_4 = 0.1$ , ActEE and HREE are the accelerometric and heart rate components of BEE respectively calculated by the Actiheart system in  $\text{J}\cdot\text{min}^{-1}$  as:

$$\text{ActEE} = 0.21 * \text{cpm} + 77 + 0 * \text{cpm} * \text{age} + 0 * \text{height} + 0 * \text{BMI} + 21$$

$$\text{HREE} = 5.5 * \text{HRaS} + 1.2 * \text{HRas} + 16 * \text{age} + 0 * \text{height} + 0 * \text{BMI} + (-94)$$

Minute averaged data was taken from each minute of each of the three minute resting and treadmill walking periods. The minute averaged Actiheart derived BEE estimates were plotted against their respective minute averaged Oxycon indirect calorimetric measurements of BEE, and the data was subjected to statistical analysis using linear regression and linear correlation in Excel software (Computer Software, Washington, USA. Microsoft v. 14.0, 2010). The plots and statistical analyses were carried out individually for each participant and for the group data.

## 2.3 Results

Anthropometric details for the 6 men who participated in this study are given in *Table 2-1*. All participants completed the 15 minute protocol without any adverse effect. Actiheart and Oxycon Mobile data were recorded successfully in each participant and no data was lost. No evidence of mechanical or electrical interference in the Actiheart signal from the Oxycon Mobile system was noted during the study. When compared with simultaneous BEE measurements made by indirect calorimetry, the Actiheart system was found to accurately predict BEE over a range of resting and treadmill walking conditions in this study.

*Table 2-1:* Participants' characteristics.

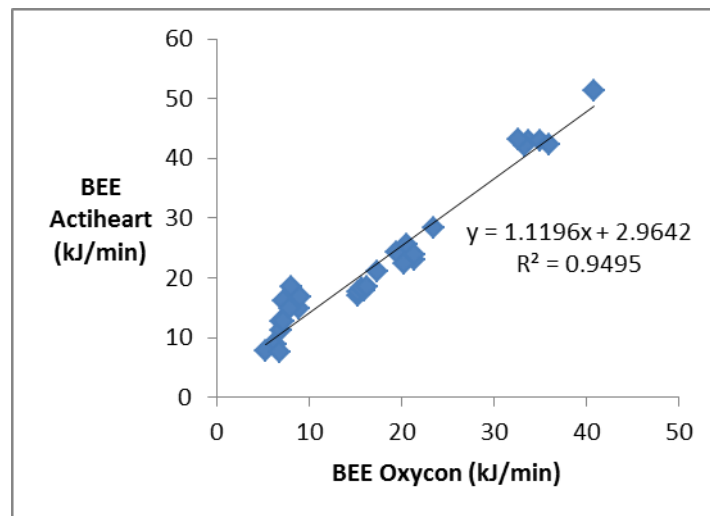
Participant	Age (yrs)	Height (cm)	Body weight (kg)	BMI (kg.m <sup>-2</sup> )
M1	37	170	75	25
M2	28	178	70	22
M3	40	190	97	26
M4	34	177	84	26
M5	31	168	78	27
M6	36	173	76	25
Mean	34.3	1.76	80.0	25.2
SD	4.3	0.08	9.5	1.7
Range	28 - 40	168 - 190	70 - 97	22 - 27

Descriptive statistics are presented in *Table 2-2*. The Actiheart derived estimates of BEE correlated very strongly with the indirect calorimetric measurements of BEE obtained from the Oxycon Mobile system under conditions ranging from rest to walking at 7 km.hr<sup>-1</sup>. For the group data, the highest correlation coefficient ( $R^2 = 0.9495$ ) was noted when only the 3<sup>rd</sup> minute of data was included from each participant and when the correlation statistic did not specify that the regression line must pass through the origin. Small reductions in the correlation coefficient occurred when the correlation statistic specified that the regression line must pass through the origin ( $R^2 = 0.9334$ ) and when all available data were included ( $R^2 = 0.9422$ ). Furthermore, stipulating that the regression line must pass through the origin had only a small effect on the regression line and linear equation (compare *Figure 2-3* and *Figure 2-4*).

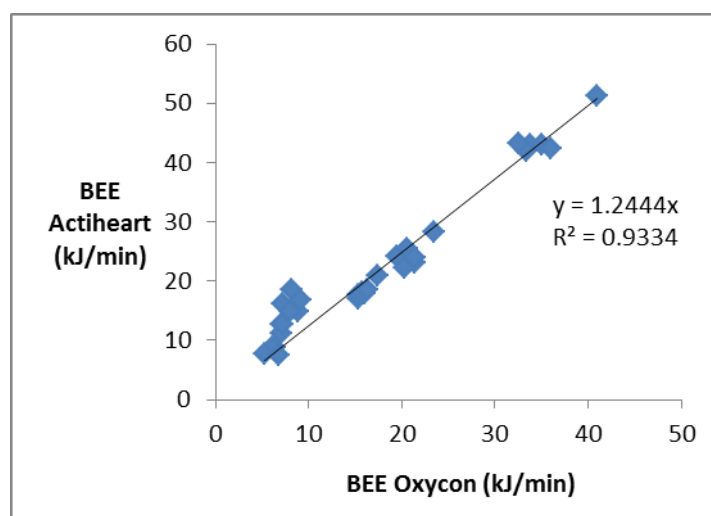
**Table 2-2:** Linear regression and correlation statistics showing relationship between Actiheart BEE estimates and BEE measurements made by indirect calorimetry during resting conditions and low to moderate treadmill walking in 6 healthy men.

Participant	3 <sup>rd</sup> minute data only. Line through origin (0,0)	3 <sup>rd</sup> minute data only. Line not through origin (not through 0,0)	All data. Line not through origin (not through 0,0)
M1	$R^2 = 0.9196$ ; N = 5 $Y = 1.2755 * X$	$R^2 = 0.9404$ ; N = 5 $Y = 1.1319 * + 3.2317$	$R^2 = 0.9517$ ; N = 15 $Y = 1.1774 * + 1.873$
M2	$R^2 = 0.9559$ ; N = 5 $Y = 1.2009 * X$	$R^2 = 0.9632$ ; N = 5 $Y = 1.1167 * + 1.9805$	$R^2 = 0.9666$ ; N = 15 $Y = 1.0539 * + 2.854$
M3	$R^2 = 0.9471$ ; N = 5 $Y = 1.232 * X$	$R^2 = 0.9571$ ; N = 5 $Y = 1.133 * + 2.231$	$R^2 = 0.9657$ ; N = 15 $Y = 1.0841 * + 2.8545$
M4	$R^2 = 0.904$ ; N = 5 $Y = 1.2744 * X$	$R^2 = 0.9568$ ; N = 5 $Y = 1.0637 * + 5.7458$	$R^2 = 0.9591$ ; N = 15 $Y = 1.104 * + 4.8934$
M5	$R^2 = 0.9661$ ; N = 5 $Y = 1.3024 X$	$R^2 = 0.974$ ; N = 5 $Y = 1.2082 * + 2.0792$	$R^2 = 0.9469$ ; N = 15 $Y = 1.3165 * + 0.4771$
M6	$R^2 = 0.9412$ ; N = 5 $Y = 1.1836 * X$	$R^2 = 0.9521$ ; N = 5 $Y = 1.0831 * + 2.4102$	$R^2 = 0.946$ ; N = 15 $Y = 1.0256 * + 3.2883$
Group data	$R^2 = 0.9334$ ; N = 30 $Y = 1.2444 * X$	$R^2 = 0.9495$ ; N = 30 $Y = 1.1196 * + 2.9642$	$R^2 = 0.9422$ ; N = 90 $Y = 1.1211 * + 2.7813$

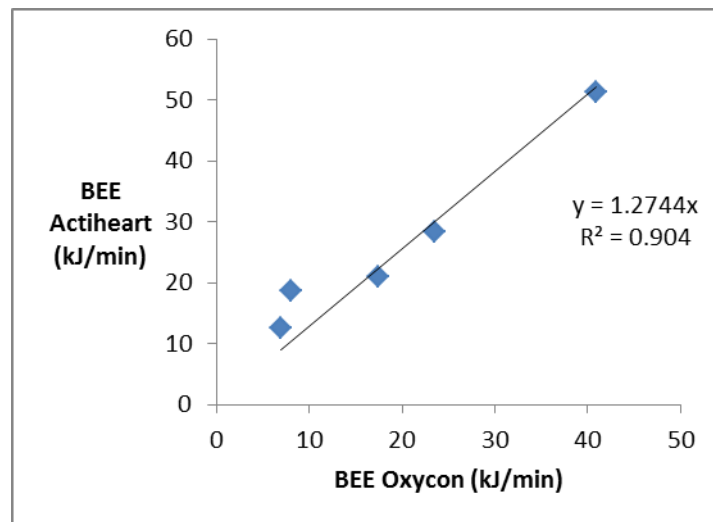
High levels of correlation were also evident in the data from each individual participant. The lowest observed correlation coefficient occurred in participant M4 when only the third minute of data was used and the correlation statistic specified that the regression line must pass through the origin. However, even in this worst case, a good level of correlation was present with  $R^2 = 0.904$  (refer to **Table 2-2** and **Figure 2-5**). The highest observed correlation coefficient ( $R^2 = 0.974$ ) occurred in participant M5 when only the third minute of data was used and the correlation statistic did not specify that the regression line must pass through the origin (refer to **Table 2-2** and **Figure 2-6**).



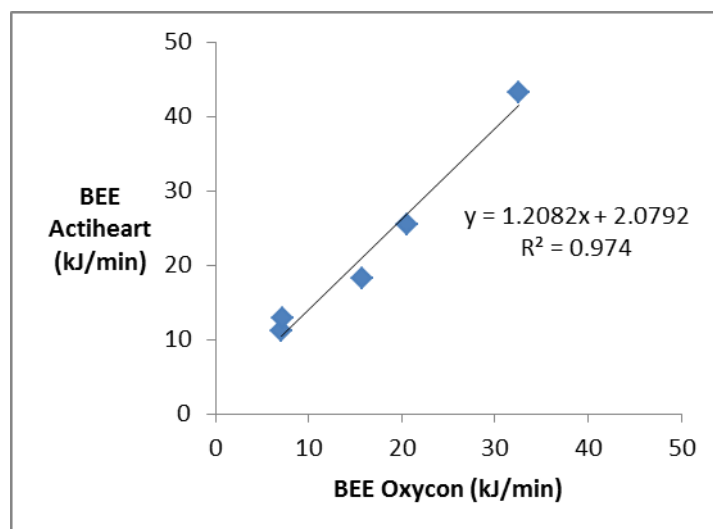
**Figure 2-3:** Relationship between actigraphic estimates of body energy expenditure (BEE) and BEE measured by indirect calorimetry (Oxycon Mobile) during rest (sitting and standing) and during treadmill walking at 3, 5 and 7 km.hr<sup>-1</sup> in 6 participants. Only the third minute of data for each resting and walking condition was used. Linear regression and correlation statistics did not specify that the regression line must pass through the origin (0,0).



**Figure 2-4:** Relationship between actigraphic estimates of body energy expenditure (BEE) and BEE measured by indirect calorimetry (Oxycon Mobile) during rest (sitting and standing) and during treadmill walking at 3, 5 and 7 km.hr<sup>-1</sup> in 6 participants. Only the third minute of data for each resting and walking condition was used. Linear regression and correlation statistics specified that the regression line must pass through the origin (0,0).



**Figure 2-5:** Relationship between actigraphic estimates of body energy expenditure (BEE) and BEE measured by indirect calorimetry (Oxycon Mobile) during rest (sitting and standing) and during treadmill walking at 3, 5 and 7 km.hr<sup>-1</sup> in one participant (M 4). Only the third minute of data for each resting and walking condition was used. Linear regression and correlation statistics specified that the regression line must pass through the origin (0,0).



**Figure 2-6:** Relationship between actigraphic estimates of body energy expenditure (BEE) and BEE measured by indirect calorimetry (Oxycon Mobile) during rest (sitting and standing) and during treadmill walking at 3, 5 and 7 km.hr<sup>-1</sup> in one participant (M 5). Only the third minute of data for each resting and walking condition was used. Linear regression and correlation statistics did not specify that the regression line must pass through the origin (0,0).



## 2.4 Discussion

Small noninvasive electronic devices such as the Actiheart have been developed in recent years to enable accurate minute - by - minute estimation of BEE from combined recordings of actigraphic and heart rate data (Brage *et al.*, 2004). The multi-sensor actigraphic and heart rate features of the Actiheart system have been shown to provide superior estimates of BEE under free-living conditions than offered by actigraphy alone (Barreira *et al.*, 2009) or heart rate alone (Corder *et al.*, 2005). The ability of the Actiheart system to accurately estimate BEE has also been demonstrated with a range of different types of exercise and physical activity including treadmill exercise (Barriera *et al.*, 2009; Brage *et al.*, 2007; Crouter *et al.*, 2008; Thompson *et al.*, 2006; Zakeri *et al.*, 2008). The results of the present study support these findings and demonstrated that the Actiheart system provided accurate estimates of BEE in normal male participants during resting conditions and during low to moderate exercise with treadmill walking at 3, 5 and 7 km.hr<sup>-1</sup> when one minute recording epochs were used. Whether shorter duration recording epochs would result in reduced BEE accuracy is not known. The present study also demonstrated that the Actiheart system gave accurate estimates of BEE when a group based equation (Brage *et al.*, 2007) was used instead of the time consuming process of individually calibrating each experimental participant with graded exercise workloads. This finding supports the study by Brage *et al.* (2007) who reported that individual calibration did not increase the accuracy of Actiheart based BEE estimates compared to Actiheart based BEE estimates derived with group based equations in people undergoing treadmill exercise.

Some researchers have commented that the accuracy of Actiheart BEE estimates is diminished at low levels of physical activity (Zakeri *et al.*, 2008). However, there was no evidence of a fixed or relative bias in Actiheart estimates of BEE observed at low exercise intensities in the present study. Indeed, as shown in *Figures 2-3* and *2-4*, the linear correlation coefficient for the group data was only slightly affected when calculation of the linear regression and correlation statistics specified that the regression line must pass through the origin (0,0). This implies that the high observed level of correlation continued down to zero levels of BEE. These findings support the study by Crouter *et al.* (2008) who reported strong correlation between Actiheart based estimates of BEE and indirect calorimetric measurements of BEE during 18 physical activities ranging from rest to activities of moderate intensity.

The correlation coefficient for the group data improved slightly when the group data set was reduced to include only data from the third minute of each level of exercise. Such an effect may signify the need to allow several minutes for cardiorespiratory function and  $\text{VO}_2$  measurements to re-equilibrate when workload is changed (Astrand and Rodahl, 1977).

In conclusion, BEE estimates derived from an Actiheart 4 (AH 4) system using the group based equations calculated from combined heart rate and 3 dimensional movement data in six healthy men were shown to be accurate when compared with simultaneous BEE measurements determined by indirect calorimetry ( $\text{VO}_2$ ) under resting conditions (sitting and standing) and during treadmill walking at 3, 5 and 7  $\text{km}\cdot\text{hr}^{-1}$ . This supports the findings of other studies. The present study confirmed the report by a previous study that the Actiheart continues to provide accurate BEE estimates when a group based equation was used instead of the time consuming process of individually calibrating each experimental participant with graded exercise workloads. The current study also found that the Mobile Oxycon system did

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not interfere mechanically or electrically with the proper and accurate functioning of the Actiheart when the Oxycon equipment was worn on the participant's back. However, this preliminary study only investigated treadmill walking and more research needs to be carried out to determine whether the accuracy of Actiheart BEE estimates is influenced by different types of exercise involving different body movements and different large muscle groups.

## **Chapter 3      Effects of Different Types of Exercise on the Accuracy of Actiheart Estimates of BEE in Healthy Participants**

### **3.1 Introduction**

Several accelerometric devices are currently commercially available for indirectly estimating BEE. Of these devices, the Actiheart system appears to offer the most accurate estimates of BEE (Barreira *et al.*, 2009; Corder *et al.*, 2005; Thompson *et al.*, 2006). Such superior accuracy stems from the fact that the Actiheart system utilizes measurements of heart rate and body movement. These multi-sensor features have been shown to provide better estimates of BEE than offered by actigraphy or heart rate alone (Barreira *et al.*, 2009; Brage *et al.*, 2004; Corder *et al.*, 2005).

A number of studies have demonstrated that the Actiheart system can accurately estimate BEE during a range of different types of physical activities (Barreira *et al.*, 2009; Brage *et al.*, 2007; Corder *et al.*, 2005; Crouter *et al.*, 2008; Thompson *et al.*, 2006; Zakeri *et al.*, 2008). However, many of these activities (especially walking and running) make only a minor contribution to the total daily BEE (Baptista *et al.*, 2012; Levine, 2004). In contrast, little is known regarding the accuracy of Actiheart based estimates of BEE during common everyday daily activities that predominantly involve the arms and upper torso. Theoretically, Actiheart accuracy may be influenced by the type of body movement involved in the physical activity for several reasons. First, arm exercise is known to elicit higher heart rate responses than leg based exercise at equivalent workloads and levels of oxygen consumption (Taguchi and Horvath, 1987; Tulppo *et al.*, 1999; Vokac *et al.*, 1975). This difference could potentially impair the Actiheart's ability to accurately estimate BEE during arm based physical activities. Second, many researchers have noted that the ability of motion sensors to detect physical

activity is influenced by the type of body movement (Bassett *et al.*, 2000; Brage *et al.*, 2005; Brage *et al.*, 2004; Corder *et al.*, 2005; Ekelund *et al.*, 2001; Eston *et al.*, 1998; Hendelman *et al.*, 2000; Meijer *et al.*, 1989; Thompson *et al.*, 2006; Westerterp, 1999; Yngve *et al.*, 2003). In view of these concerns, a study was conducted to compare the accuracy of Actiheart based estimates of BEE during arm based activities and during other forms of physical activity at matched mechanical workloads.

### **3.1.1 Aim of the Study**

The aim of this study was to evaluate the accuracy of the Actiheart based estimates of BEE during low and moderate intensity physical activities that utilised different body movements and different muscle groups under matched mechanical workloads involving bicycle and arm ergometry, and during matched levels of treadmill walking. Particular attention was given to whether higher heart rate responses occurred during arm based exercise, and whether this adversely impacted on the accuracy of Actiheart based estimates of BEE.

## 3.2 Materials and Methods

This study was approved by the University of New England Human Research Ethics Committee (Approval No. HE10/186, Valid to 05/11/2011). Each participant gave informed consent prior to commencement of the study and was instructed that they could withdraw from the study at any time without penalty.

### 3.2.1 Participants

Ten healthy adult male volunteers were recruited for this study. All were physically active but none were high performance athletes. All of the participants were non-smokers, without known current disease or physical disability. None of the participants had been ill during the past month and none were taking any medications at the time of the study. All were from the University of New England student population and were approached and invited by the author to participate in the study after they successfully completed a basic PAR-Q physical activity readiness questionnaire (Physical Activity Readiness Questionnaire, 2002).

### 3.2.2 Equipment

BEE was estimated with an Actiheart 4 (AH4) system placed over the participant's chest as previously described (refer to *section 2.2.3.1 Equipment calibration and participant instrumentation*). In addition, indirect calorimetric measurements of BEE were obtained from oxygen consumption using a telemetric Oxycon mobile system (Oxycon Mobile® Erich Jaeger, Viasys Healthcare, Germany) as previously described (refer to *section 2.2.2.2 Oxycon mobile*).

### 3.2.2.1 Exercise Equipment

Each participant underwent three different modes of exercise in the laboratory with the following equipment: a Cosmos treadmill (Wood Way® Waukesha, Wisconsin USA, model no pro XL), an arm ergometer (Monark exercise AB, model 881E, Sewed) and a cycling ergometer (Monark exercise AB, model 828E, Sewed).

### 3.2.2.2 Body Energy Expenditure Calibrations and Participant

#### Instrumentation

With the Actiheart system properly positioned, the sleeping heart rate was estimated following the Actiheart user manual instructions (CamNtech Neurotechnology Ltd, Cambridge UK, user manual. v 4.0.35. 2010). Calibrations for the Oxycon mobile system's carbon dioxide and oxygen analysers and air flow turbine were carried out following the manufacturer's instructions (Oxycon Mobile® Erich Jaeger, Viasys Healthcare, Hochberg Germany. user manual. v 5.2. 2007) prior to instrumenting the participant with the Oxycon mobile system. These calibration procedures have also been previously discussed in detail (refer to *section 2.2.3.1 Equipment calibration and participant instrumentation*).

### **3.2.2.3 Exercise Equipment Tests Prior to the Study**

Several days prior to the study day, each participant familiarised themselves with the exercise equipment by walking on the treadmill, arm cranking using the arm ergometer and cycling on the bicycle ergometer. During this time, each participant's optimal seat height was measured for the bicycle ergometer, as was the optimal position (height and horizontal distance) of the arm ergometer from the participant. The calibration of the arm ergometer and the bicycle ergometer was checked prior to the study as instructed by the manufacturer's user manuals (Monark Ergomedic 881E manual, 2008; Monark Ergomedic 828E manual, 2008).

### **3.2.2.4 Exercise Equipment Tests During the Study**

During the period of the test, the cadence was constantly shown on a display on the arm ergometer and the bicycle ergometer, and this was visible to both the participant and the investigator. All participants were instructed to keep the cadence within  $\pm 3$  revolutions per minute (rpm) of the target value. The braking force on the arm and bicycle ergometers changed slightly over time due to increased temperature from friction. Therefore, one investigator checked, and if necessary reset, the braking force every minute to ensure that the cadence remained within the range of  $\pm 3$  rpm of the target value.

## **3.2.3 Experimental Protocol**

Each participant was asked to avoid eating or drinking (except water) or doing any high level physical activities for at least 2 hours before arriving at the laboratory. The three exercise regimes were carried on the same day for each participant in random order. For the



purposes of this study, it was assumed that the mechanical efficiency of arm exercise was sufficiently similar to that of leg exercise so that a given ergometric workload in kilopond meters per minute ( $\text{kpm}\cdot\text{min}^{-1}$ ) imposed approximately matching levels of  $\text{VO}_2$  responses during exercise with a bicycle ergometer and an arm ergometer. Ergometric workloads on the bicycle and arm ergometers which approximately matched low and moderate intensity treadmill walking speeds (zero horizontal incline) of 3, 5 and 7  $\text{km}\cdot\text{hr}^{-1}$  were then determined in the following manner. First, bicycle ergometric workloads of equivalent BEE to treadmill walking at 5 and 7  $\text{km}\cdot\text{hr}^{-1}$  were derived from conversion estimates supplied by Astrand and Rodahl (1977). However, these conversion estimates were inappropriate for treadmill speeds below 5  $\text{km}\cdot\text{hr}^{-1}$  and suggested that the bicycle ergometric equivalent for treadmill speeds of 3  $\text{km}\cdot\text{hr}^{-1}$  would be 0  $\text{kpm}\cdot\text{min}^{-1}$ . An ergometric value half-way between 0 and 300  $\text{kpm}\cdot\text{min}^{-1}$  (i.e. 150  $\text{kpm}\cdot\text{min}^{-1}$ ) was therefore chosen to better represent a treadmill speed of 3  $\text{km}\cdot\text{hr}^{-1}$ . The resultant matched workloads for the three different modes of exercise are given in **Table 3-1**.

**Table 3-1:** Exercise intensities for three modes of exercise used.

Type of Exercise	Exercise Intensity		
	Lowest	Intermediate	Highest
Treadmill walking	3 $\text{km}\cdot\text{hr}^{-1}$	5 $\text{km}\cdot\text{hr}^{-1}$	7 $\text{km}\cdot\text{hr}^{-1}$
Bicycle ergometer	150 $\text{kpm}\cdot\text{min}^{-1}$	300 $\text{kpm}\cdot\text{min}^{-1}$	600 $\text{kpm}\cdot\text{min}^{-1}$
Arm ergometer	150 $\text{kpm}\cdot\text{min}^{-1}$	300 $\text{kpm}\cdot\text{min}^{-1}$	600 $\text{kpm}\cdot\text{min}^{-1}$

### 3.2.3.1 Rest and Exercise Protocol

Once all the equipment was setup correctly and the participant was correctly instrumented, the protocol consisted of:

For treadmill exercise: 3 minutes rest, followed by 3 minutes treadmill walking at 3 km.hr<sup>-1</sup>, followed by 3 minutes treadmill walking at 5 km.hr<sup>-1</sup>, followed by 3 minutes treadmill walking at 7 km.hr<sup>-1</sup>.

For bicycle ergometer exercise: 3 minutes rest, followed by 3 minutes of cycling at 150 kpm.min<sup>-1</sup>, followed by 3 minutes of cycling at 300 kpm.min<sup>-1</sup>, followed by 3 minutes of cycling at 600 kpm.min<sup>-1</sup>.

For arm ergometer exercise: 3 minutes rest, followed by 3 minutes of arm cranking at 150 kpm.min<sup>-1</sup>, followed by 3 minutes of arm cranking at 300 kpm.min<sup>-1</sup>, followed by 3 minutes of arm cranking at 600 kpm.min<sup>-1</sup>.

The three modes of exercise were performed in random order. At least two hours rest was given between each mode of exercise to enable the participants' heart rate to return to within 10 bpm of their original standing heart rate. This procedure was consistent with the Oxycon mobile operating instructions (Oxycon Mobile® Erich Jaeger, Viasys Healthcare, Hochberg Germany. user manual. v 5.2, 2007).

### 3.2.4 Measurements

Each participant's height and body weight (bare foot and wearing only light clothes) were respectively measured to the nearest 0.5 cm using a standard stadiometer and to the nearest tenth of kilogram by using a body composition monitor with scales (Omron Healthcare Co. Ltd, Japan, model HBF-500). Body mass index (BMI) for each participant was calculated according to the formula:  $BMI = \text{body weight} \div \text{height}^2$  (kg. m<sup>-2</sup>).

### 3.2.5 Data Analysis

Heart rate and body movement data recorded with the Actiheart system were transferred onto a lap top computer using an Actiheart reader system (CamNtech Neurotechnology Ltd, Cambridge UK, serial no 320208). Actiheart system software (CamNtech Neurotechnology Ltd, Cambridge UK. software v.4.0.89) was used to analyse the recorded Actiheart data over 60 second epochs. The captured data was then analysed with a validated group-based branched-equation model (Brage *et al.*, 2007) which has been previously discussed in detail (refer to *section 2.2.4 Data Analysis*). Data collected by the Oxycon mobile system was transferred to a lap top computer and analysed using dedicated software (CardinalHealth, Hochberg, Germany. JLAB software v. 5.22.1). Oxygen consumption based measurements of BEE were calculated each minute, and corresponding BEE values were calculated in kJ.min<sup>-1</sup> after correction for changes in the (RER) (Fox and Mathews, 1981).

Actiheart and Oxycon mobile derived measurements of BEE were each averaged over the third minute of rest and the third minute of each level of activity. Data analysis was performed with Excel software (Computer Software, Washington, USA. Microsoft v. 14.0, 2010). All data are reported as means  $\pm$  1 SD unless specified otherwise. Actiheart based estimates of BEE were compared with simultaneous indirect calorimetric Oxycon mobile measurements of BEE for the four different levels of exercises intensities and each of the three different modes of exercise (treadmill, arm ergometer and bicycle ergometer).

### 3.2.6 Statistical Analysis

Statistical analysis of the data was performed with SPSS software (IBM Corp, Amonk, NY, USA. *SPSS Statistic for windows* v. 19.0. 2010). One-way analysis variance (ANOVA) and the least significant difference (LSD) test were used to compare  $VO_2$  at equivalent levels of exercise intensity for the 3 different exercise modes. Paired Student's *t* tests were used to determine whether there were differences between Actiheart based BEE estimates and simultaneous measurements of BEE determined by indirect calorimetry. Similarly, comparisons were made for Oxycon mobile based measurements of RER and BEE, and the Actiheart based measures of heart rate and BEE. For each of these tests, the alpha level was set at 0.05 (2 tailed) to indicate statistical significance.

### 3.3 Results

The anthropometric characteristics of the ten adult male participants are provided as means  $\pm$  SD in **Table 3.2**. Each participant successfully completed each component of the exercise protocols for each of the three different exercise modes without adverse effects.

**Table 3-2:** Anthropometric characteristics.

Variables	Mean $\pm$ SD
Age (yrs)	29.2 $\pm$ 3.7
Height (cm)	176 $\pm$ 5.7
Body weight (kg)	74.7 $\pm$ 2.4
BMI (kg/m <sup>2</sup> )	22.5 $\pm$ 1.6

As shown in **Table 3-3**,  $V_{O_2}$  measurements between the three modes of exercise were closely matched at any given workload intensity ( $p > 0.05$ ). In addition, indirect calorimetric measurements of BEE, which were derived from these  $V_{O_2}$  measurements, were also all closely matched ( $p > 0.05$ ) except at the highest workload intensity ( $p < 0.05$ ) as shown in **Table 3-4** and **Figure 3-1**. However, at the highest workload indirect calorimetric based measurements of BEE were significantly lower ( $p < 0.05$ ) during bicycle ergometry than during arm ergometry or treadmill walking (refer to **Table 3-4**), and this discrepancy was also noted in the RER (refer to **Table 3-5**).

**Table 3-3:**  $\text{VO}_2$  ( $\text{ml.kg}^{-1}.\text{min}^{-1}$ ) during three different exercises modes at four different levels of exercise intensity. Data are means  $\pm$  1 SD for 10 healthy men.

Exercise intensity	Treadmill	Arm	Bike
Rest	$4.5 \pm 0.9$	$4.4 \pm 0.7$	$4.3 \pm 0.8$
Lowest	$9.8 \pm 1.1$	$9.6 \pm 2.1$	$9 \pm 1.2$
Intermediate	$13.8 \pm 1.2$	$13.3 \pm 1.9$	$13.1 \pm 1.5$
Highest	$23 \pm 1.4$	$22.1 \pm 1.1$	$21.5 \pm 2.7$

Lowest, intermediate and highest treadmill walking exercise intensities equaled 3, 5 and 7  $\text{km.hr}^{-1}$ , whereas lowest, intermediate and highest arm and bicycle ergometer exercise intensities equaled 150  $\text{kpm.min}^{-1}$ , 300  $\text{kpm.min}^{-1}$  and 600  $\text{kpm.min}^{-1}$ . Note that there was no statistically significant difference ( $p < 0.05$ , ANOVA) between the three modes of exercise for any given workload intensity.

**Table 3-4:** Oxycon mobile measurements of the BEE ( $\text{kJ.min}^{-1}$ ) during three difference exercise modes at four different level of exercise intensity. Data are means  $\pm$  1 SD for 10 healthy men.

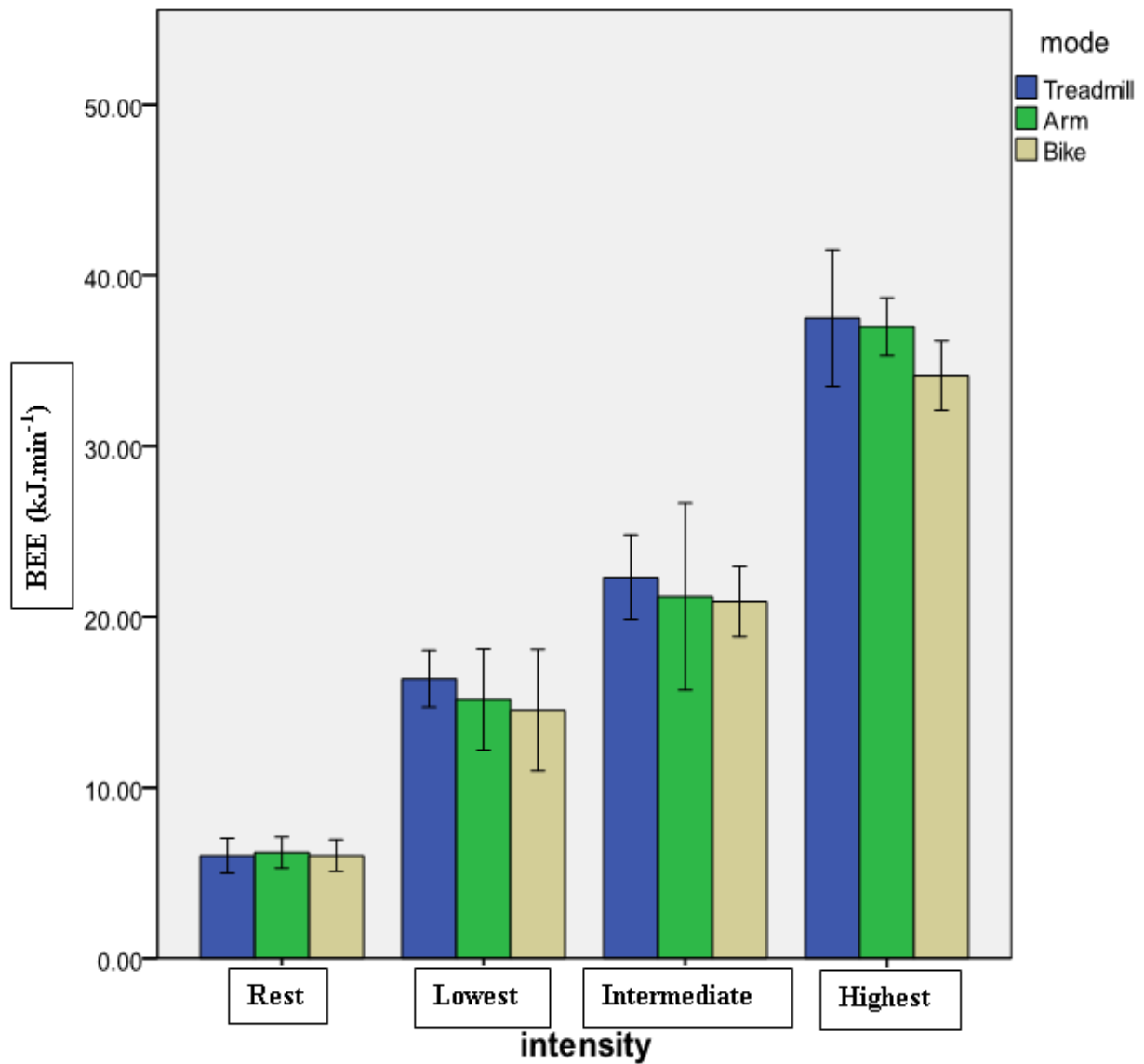
Exercise intensity	Treadmill	Arm	Bike
Rest	$6 \pm 1.1$	$6.2 \pm 0.9$	$6 \pm 0.9$
Lowest	$16.4 \pm 1.7$	$15.1 \pm 3$	$14.5 \pm 3.6$
Intermediate	$22.33 \pm 2.5$	$21.2 \pm 5.5$	$20.9 \pm 2.1$
Highest	$*37.5 \pm 4$	$*37 \pm 1.7$	$34.1 \pm 2.1$

Lowest, intermediate and highest treadmill walking exercise intensities equaled 3, 5 and 7  $\text{km.hr}^{-1}$ , whereas lowest, intermediate and highest arm and bicycle ergometer exercise intensities equaled 150  $\text{kpm/min}$ , 300  $\text{kpm/min}$  and 600  $\text{kpm.min}^{-1}$ . \* denotes  $p < 0.05$  from bicycle ergometer exercise (ANOVA and LSD).

**Table 3-5:** (RER) was measured via indirect calorimetry during three different exercises modes at four different levels of exercise intensity. Data are means  $\pm$  1 SD for 10 healthy men.

RER	Treadmill	Arm	Bike
Rest	$0.72 \pm 0.018$	$0.75 \pm 0.017$	$0.73 \pm 0.019$
Lowest	$0.80 \pm 0.022$	$0.81 \pm 0.03$	$0.78 \pm 0.027$
Intermediate	$0.87 \pm 0.026$	$0.85 \pm 0.049$	$0.84 \pm 0.022$
Highest	$*1 \pm 0.08$	$*0.98 \pm 0.024$	$0.90 \pm 0.025$

Lowest, intermediate and highest treadmill walking exercise intensities equaled 3, 5 and 7  $\text{km.hr}^{-1}$ , whereas lowest, intermediate and highest arm and bicycle ergometer exercise intensities equaled 150  $\text{kpm.min}^{-1}$ , 300  $\text{kpm.min}^{-1}$  and 600  $\text{kpm.min}^{-1}$ . \* denotes  $p < 0.05$  from bicycle ergometer exercise data (ANOVA and LSD).



**Figure 3-1:** Indirect calorimetric measurements of body energy expenditure made with the Oxycon mobile system during three different exercise modes at rest and three different levels of exercise intensity. Data are means  $\pm$  1 SD (horizontal bars) from 10 healthy men. Lowest exercise intensity – 3 km.hr<sup>-1</sup> (treadmill) and 150 kpm.min<sup>-1</sup> (ergometers). Intermediate exercise intensity – 5 km.hr<sup>-1</sup> (treadmill) and 300 kpm.min<sup>-1</sup> (ergometers). Highest exercise intensity – 7 km.hr<sup>-1</sup> (treadmill) and 600 kpm.min<sup>-1</sup> (ergometers).

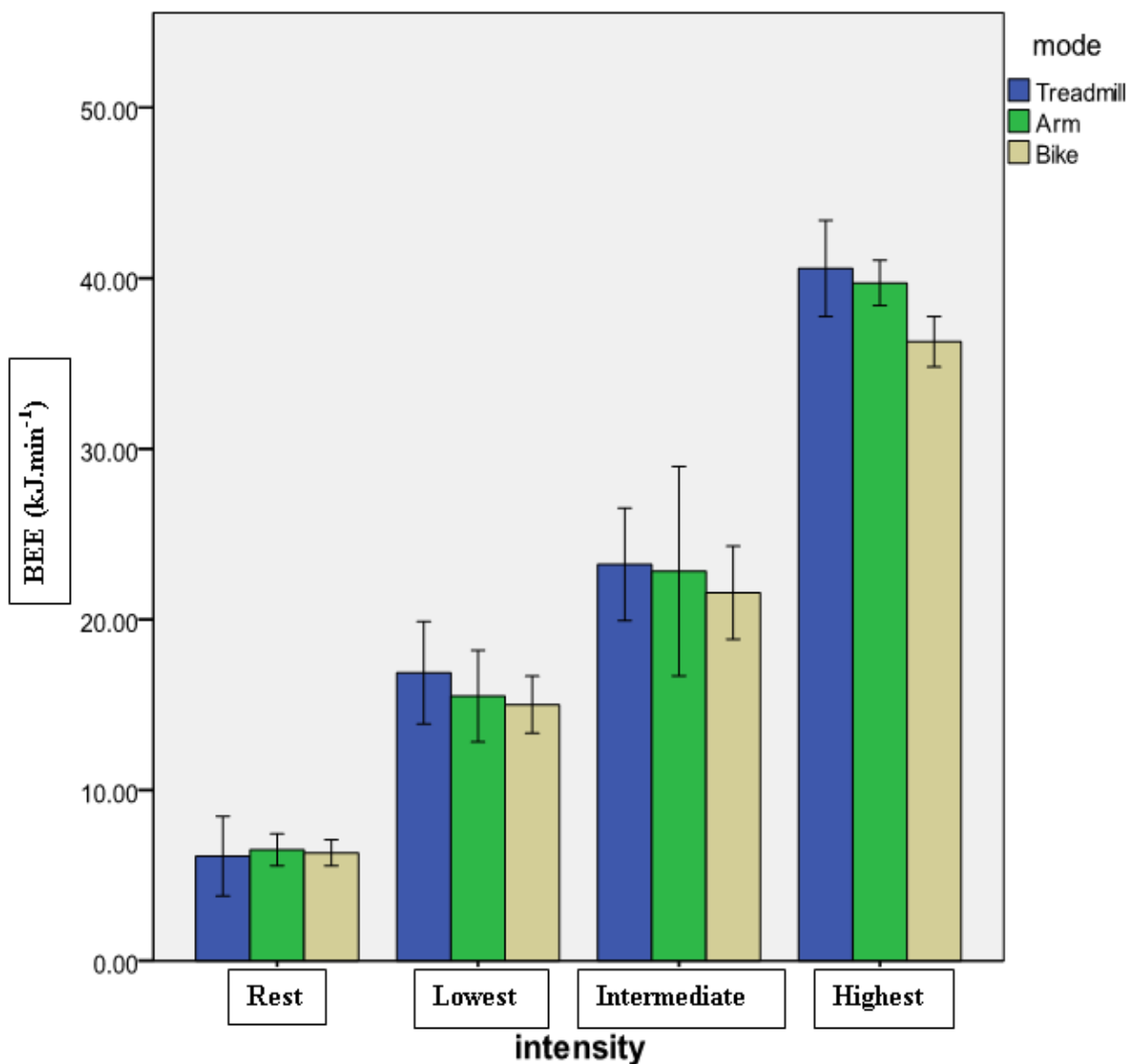
Actiheart based estimates of BEE between the three modes of exercise were closely matched at rest and any given workload intensity, except for the highest workload where BEE during bicycle ergometry was significantly lower ( $p < 0.05$ ) than during arm ergometry or treadmill walking (refer to **Table 3-6** and **Figure 3-2**).

**Table 3-6:** Actiheart based estimates of BEE ( $\text{kJ}\cdot\text{min}^{-1}$ ) during three different exercise modes at rest and three different levels of exercise intensities. Data are means  $\pm$  1 SD for 10 healthy men.

Exercise intensity	Treadmill	Arm	Bike
Rest	$6.1 \pm 2.3$	$6.5 \pm 0.9$	$6.3 \pm 0.8$
Lowest	$16.9 \pm 3$	$15.5 \pm 2.7$	$15 \pm 1.7$
Intermediate	$23.23 \pm 3.3$	$22.8 \pm 6.1$	$21.6 \pm 2.7$
Highest	$*40.57 \pm 2.81$	$*39.7 \pm 1.32$	$36.2 \pm 1.5$

Lowest, intermediate and highest treadmill walking exercise intensities equaled 3, 5 and 7  $\text{km}\cdot\text{hr}^{-1}$ , whereas lowest, intermediate and highest arm and bicycle ergometer exercise intensities equaled 150  $\text{kpm}\cdot\text{min}^{-1}$ , 300  $\text{kpm}\cdot\text{min}^{-1}$  and 600  $\text{kpm}\cdot\text{min}^{-1}$ . \* denotes  $p < 0.05$  from bicycle ergometer exercise data (ANOVA and LSD).





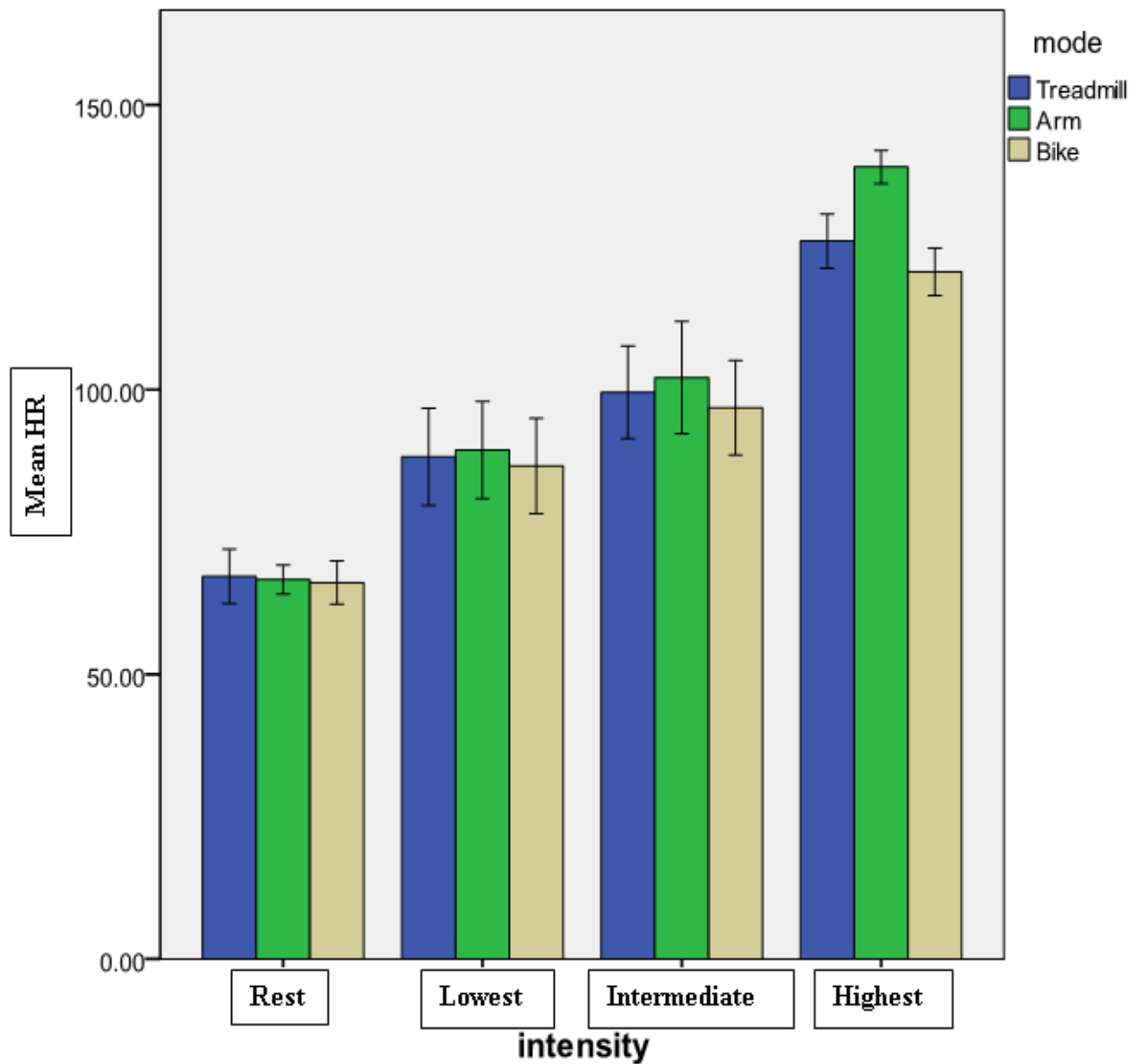
**Figure 3-2:** Estimated body energy expenditure from the Actiheart system during three different exercise modes at rest and three different levels of exercise intensity. Data are means  $\pm$  1 SD (horizontal bars) from 10 healthy men. Lowest exercise intensity – 3 km.hr<sup>-1</sup> (treadmill) and 150 kpm.min<sup>-1</sup> (ergometers). Intermediate exercise intensity – 5 km.hr<sup>-1</sup> (treadmill) and 300 kpm.min<sup>-1</sup> (ergometers). Highest exercise intensity – 7 km.hr<sup>-1</sup> (treadmill) and 600 kpm.min<sup>-1</sup> (ergometers).

ANOVA and the LSD tests failed to demonstrate significant differences during three different modes of exercise ( $p > 0.05$ ), except at the highest workload where heart rate was higher during arm exercise than during bicycle exercise or treadmill walking ( $p < 0.05$ ) (refer to *Table 3-7* and *Figure 3-3*).

**Table 3-7:** Heart rate (bpm) during three different exercises modes at rest and three different levels of exercise intensity. Data are means  $\pm$  1 SD for 10 healthy men.

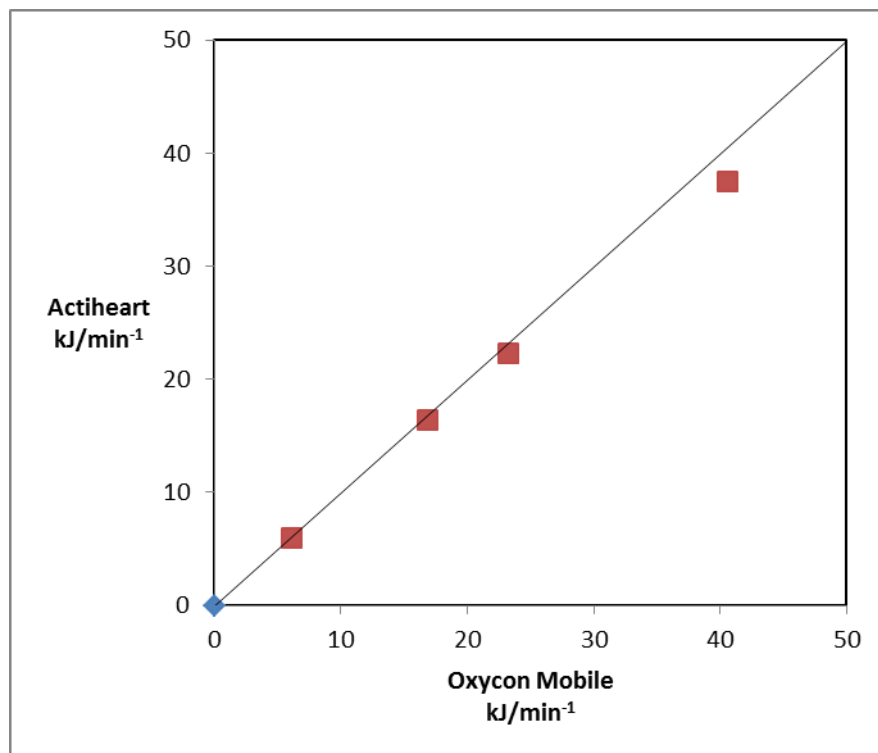
Exercise intensity	Treadmill	Arm	Bike
Rest	67.2 $\pm$ 4.8	66.6 $\pm$ 2.5	66.1 $\pm$ 3.8
Lowest	88.2 $\pm$ 8.5	89.4 $\pm$ 8.6	86.6 $\pm$ 8.4
Intermediate	99.5 $\pm$ 8.1	102.1 $\pm$ 9.9	96.8 $\pm$ 8.3
highest	*126.1 $\pm$ 4.7	139.1 $\pm$ 3	*120 $\pm$ 4.14

Lowest, intermediate and highest treadmill walking exercise intensities equaled 3, 5 and 7 km.hr<sup>-1</sup>, whereas lowest, intermediate and highest arm and bicycle ergometer exercise intensities equaled 150 kpm.min<sup>-1</sup>, 300 kpm.min<sup>-1</sup> and 600 kpm.min<sup>-1</sup>. \* denotes  $p < 0.05$  from arm ergometer exercise data (ANOVA and LSD).

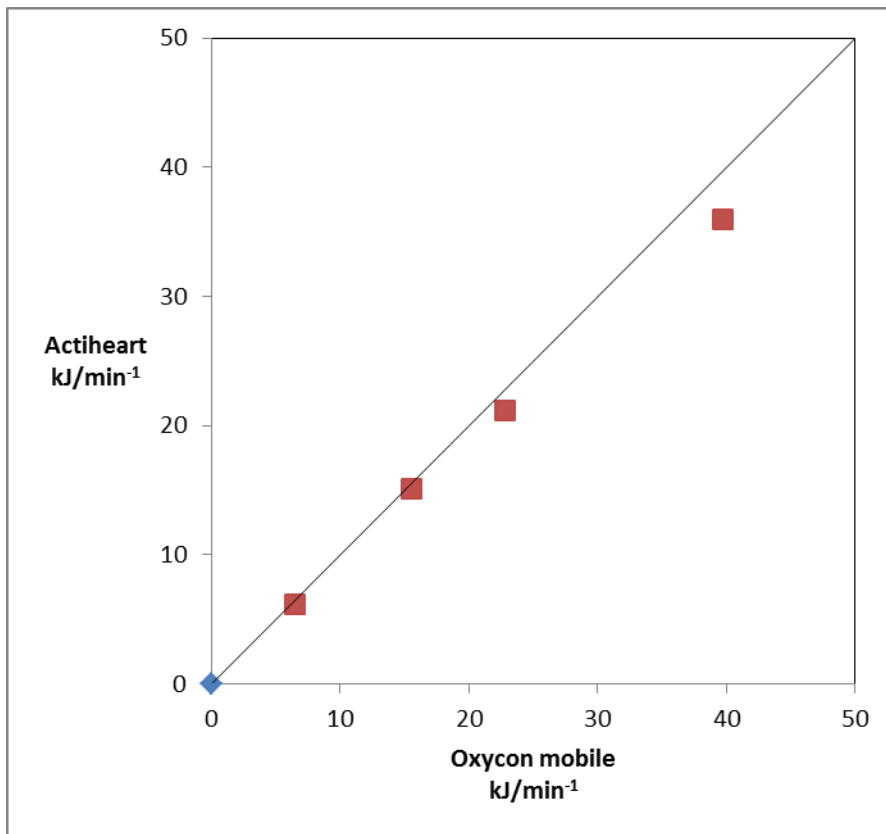


**Figure 3-3:** Heart rate during three different exercise modes at rest and three different levels of exercise intensity. Data are means  $\pm$  1 SD (horizontal bars) from 10 healthy men. Lowest exercise intensity – 3 km.hr<sup>-1</sup> (treadmill) and 150 kpm.min<sup>-1</sup> (ergometers). Intermediate exercise intensity – 5 km.hr<sup>-1</sup> (treadmill) and 300 kpm.min<sup>-1</sup> (ergometers). Highest exercise intensity – 7 km.hr<sup>-1</sup> (treadmill) and 600 kpm.min<sup>-1</sup> (ergometers).

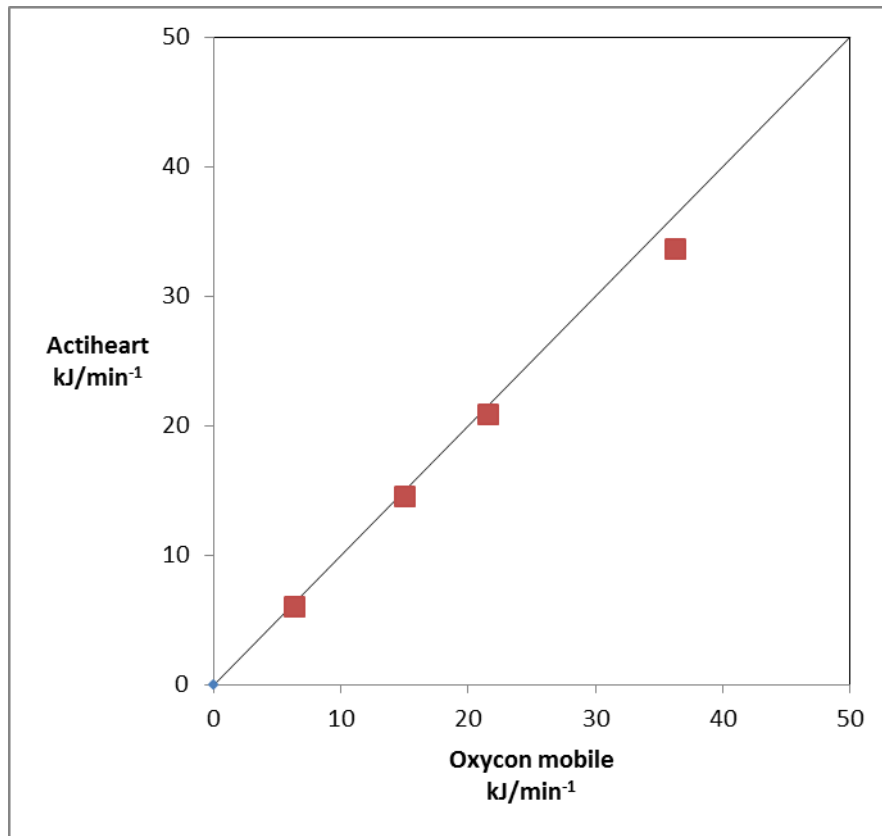
Actiheart based estimates of BEE agreed very closely with the simultaneous indirect calorimetric based measurements of BEE. This was evident under resting conditions and during each workload for each of the 3 types of exercise examined in this study (refer to *Figures 3-4, 3-5 and 3-6*), and was confirmed by paired *t*-test comparisons (refer to *Tables 3-8, 3-9 and 3-10*).



**Figure 3-4:** Relationship between Actiheart based estimates of BEE and simultaneous indirect calorimetric measurements of BEE (Oxycon Mobile) during rest (sitting) and during treadmill walking at 3, 5 and 7  $\text{km}\cdot\text{hr}^{-1}$ . Data are means from 10 healthy men. The diagonal line represents the line of identity. Note the close agreement between the Actiheart based estimates and the indirect calorimetric measurements of BEE.



**Figure 3-5:** Relationship between Actiheart based estimates of BEE and simultaneous indirect calorimetric measurements of BEE (Oxycon Mobile) during rest (sitting) and during arm ergometric exercise at 150, 300 and 600  $\text{kpm}\cdot\text{min}^{-1}$ . Data are means from 10 healthy men. The diagonal line represents the line of identity. Note the close agreement between the Actiheart based estimates and the indirect calorimetric measurements of BEE.



**Figure 3-6:** Relationship between Actiheart based estimates of BEE and simultaneous indirect calorimetric measurements of BEE (Oxycon Mobile) during rest (sitting) and during bicycle ergometric exercise at 150, 300 and 600  $\text{kpm}\cdot\text{min}^{-1}$ . Data are means from 10 healthy men. The diagonal line represents the line of identity. Note the close agreement between mean Actiheart based and the indirect calorimetric measurements of BEE.

**Table 3-8:** BEE ( $\text{kJ}\cdot\text{min}^{-1}$ ) estimated by the Actiheart system and measured by indirect calorimetry by the Oxycon mobile system in 10 healthy men during resting conditions and treadmill walking with zero incline at 3, 5 and 7  $\text{km}\cdot\text{hr}^{-1}$ .

Treadmill walking exercise intensity	Actiheart BEE ( $\text{kJ}\cdot\text{min}^{-1}$ )	Oxycon BEE ( $\text{kJ}\cdot\text{min}^{-1}$ )	Probability (paired <i>t</i> -tests)
Rest	$6.1 \pm 2.3$	$6 \pm 1.1$	0.79
Lowest	$16.9 \pm 3$	$16.4 \pm 1.7$	0.54
Intermediate	$23.2 \pm 3.3$	$22.3 \pm 2.5$	0.42
Highest	$40.6 \pm 2.8$	$37.5 \pm 4$	0.28

No significant differences were noted between the Actiheart and Oxycon based BEE measurements (all  $p < 0.05$ ).

**Table 3-9:** BEE ( $\text{kJ}\cdot\text{min}^{-1}$ ) estimated by the Actiheart system and measured by indirect calorimetry by the Oxycon mobile system in 10 healthy men during resting conditions and arm ergometry exercise at 150, 300 and 600  $\text{kpm}\cdot\text{min}^{-1}$ .

Arm ergometry exercise intensity	Actiheart BEE ( $\text{kJ}\cdot\text{min}^{-1}$ )	Oxycon BEE ( $\text{kJ}\cdot\text{min}^{-1}$ )	Probability (paired <i>t</i> -tests)
Rest	$6.5 \pm 0.9$	$6.2 \pm 0.9$	0.23
Lowest	$15.5 \pm 2.7$	$15.1 \pm 3$	0.65
Intermediate	$22.1 \pm 4$	$21.2 \pm 5.5$	0.12
Highest	$38.8 \pm 2.3$	$37.0 \pm 1.7$	0.10

No significant differences were noted between the Actiheart and Oxycon based BEE measurements (all  $p < 0.05$ ).

**Table 3-10:** BEE ( $\text{kJ}\cdot\text{min}^{-1}$ ) estimated by the Actiheart system and measured by indirect calorimetry by the Oxycon mobile system in 10 healthy men during resting conditions and bicycle ergometry exercise at 150, 300 and 600  $\text{kpm}\cdot\text{min}^{-1}$ .

Bicycle ergometry exercise intensity	Actiheart BEE ( $\text{kJ}\cdot\text{min}^{-1}$ )	Oxycon BEE ( $\text{kJ}\cdot\text{min}^{-1}$ )	Probability (paired <i>t</i> -tests)
Rest	$6.3 \pm 0.8$	$6.0 \pm 0.9$	0.12
Lowest	$15.0 \pm 1.7$	$14.5 \pm 3.6$	0.66
Intermediate	$21.6 \pm 2.7$	$20.9 \pm 2.1$	0.50
Highest	$35.6 \pm 1.9$	$34.1 \pm 2.1$	0.13

No significant differences were noted between the Actiheart and Oxycon based BEE measurements (all  $p < 0.05$ ).

## 3.4 Discussion

### 3.4.1 Introductory Comments

The primary purpose of the current study was to evaluate the accuracy of the Actiheart based estimates of BEE during physical activities that utilised different body movements and different muscle groups under matched mechanical workloads involving bicycle and arm ergometry, and during matched levels of treadmill walking. The accuracy of Actiheart based BEE estimates during low to moderate intensity arm and upper torso exercise was of particular interest because many common everyday daily activities predominantly involve the arms and upper torso, and because such activities may on theoretical grounds yield different Actiheart based BEE results than matched workloads of exercise involving the legs.

### 3.4.2 Accuracy

A major finding of this study was that the Actiheart system accurately estimated BEE for each of the modes of exercise and levels of exercise intensity studied. Thus, Actiheart based BEE estimates continued to accurately track Oxycon mobile BEE measurements during rest and each of the three levels of exercises intensity for each of the three modes of exercise.  $\text{VO}_2$  matching between the 3 types of exercise was slightly reduced at the highest workload, but even under these conditions the Actiheart continued to provide estimates of BEE which agreed closely with the simultaneous indirect calorimetric BEE measurements.

Good correlations between Actiheart based estimates of BEE and simultaneous indirect calorimetric measurements of BEE have been reported over a range of different types and intensities of physical activities (Barreira *et al.*, 2009; Brage *et al.*, 2007; Corder *et al.*,



2005; Crouter *et al.*, 2008; Thompson *et al.*, 2006; Zakeri *et al.*, 2008). However, the present study is the first to demonstrate that the accuracy of Actiheart based BEE estimates at matched mechanical workloads remains high over a range of different modes of exercises which involve different body movements and utilise different muscle groups.

Various studies have reported that motion sensors and systems that utilize combined heart rate and accelerometer inputs such as the Actiheart can underestimate BEE at higher levels of exercise intensity during running (Barreira *et al.*, 2009; Corder *et al.*, 2005; Eston *et al.*, 1998; Meijer *et al.*, 1989). Meijer *et al.* (1989) speculated that such underestimates may be due to participants restraining their body movements while running at high speeds on a treadmill. This possibility may account for the lack of underestimation in Actigraphic BEE during the highest treadmill speed in the present study because participants only walked on the treadmill. Indeed, the Actiheart system was found to accurately estimate BEE during rest and during each of the three exercise intensities for each of the three modes of exercise in the present study. This finding is consistent with the high accuracy of Actiheart based estimates of BEE reported in other studies during resting and low to moderate intensity activities (Barreira *et al.*, 2009; Brage *et al.*, 2007; Corder *et al.*, 2005; Thompson *et al.*, 2006; Zakeri *et al.*, 2008). This ability to accurately estimate BEE over a wide range of low to moderate intensity activities is a specifically designed feature of the Actiheart system which relies on combined heart rate and accelerometer inputs with software that utilizes different equations to yield optimal estimates of BEE under different intensities of physical activity (Brage *et al.*, 2007). These features are likely to have substantial clinical significance because the Actiheart system can offer accurate monitoring of patients in whom only low and moderate levels of exercise intensity are likely to be tolerated.

### 3.4.2.1 Arm Exercise

No previous study has specifically examined the accuracy of Actiheart based estimates of BEE during arm exercise protocols. There are several theoretical reasons why the accuracy of Actiheart based estimates of BEE could be reduced during arm based exercise. First, Actiheart based estimates of BEE are in part determined by the heart rate (Brage *et al.*, 2007). However, the heart rate response to arm exercise is higher than during leg based exercise at equivalent mechanical workloads and levels of oxygen consumption (Taguchi and Horvath, 1987; Tulppo *et al.*, 1999; Vokac *et al.*, 1975), and this effect could inaccurately elevate Actiheart based estimates of BEE during arm exercise.

Actiheart based estimates of BEE are also in part determined by the inputs from accelerometers which detect body movement (Brage *et al.*, 2007). However, many studies have shown that the ability of body motion sensors to detect physical activity is influenced by the type of body movements utilised during physical activity (Bassett *et al.*, 2000; Brage *et al.*, 2005; Brage *et al.*, 2004; Corder *et al.*, 2005; Ekelund *et al.*, 2001; Eston *et al.*, 1998; Meijer *et al.*, 1989; Thompson *et al.*, 2006; Westerterp, 1999; Yngve *et al.*, 2003). In addition, the ability of sensors to detect body movement and provide estimates of BEE can be influenced by where the sensors are positioned on the body in relation to the type of body movement encountered (Corder *et al.*, 2005; Eston *et al.*, 1998; Westerterp, 1999; Yngve *et al.*, 2003). Consequently, the accuracy of BEE estimates when the Actiheart is positioned on the chest could theoretically differ between arm based and leg based activities performed at comparable levels of exercise intensity. Only one study appears to have examined the effect of different body placements on the movement sensor data from the Actiheart system and this study found little placement difference in energy expenditure estimates from Actiheart

systems placed over the 3<sup>rd</sup> intercostal space and below the apex of the sternum (Brage *et al.*, 2006).

The heart rate response to 600 kpm.min<sup>-1</sup> of arm ergometry exercise was higher than during matched workloads for bicycle ergometry and treadmill walking. This confirms findings from previous studies (Taguchi and Horvath, 1987; Tulppo *et al.*, 1999; Vokac *et al.*, 1975). However, even under these conditions the Actiheart system continued to accurately estimate BEE. Indeed, the Actiheart system accurately estimated BEE for each of the modes of exercise and levels of exercise intensity studied. Thus, despite the above mentioned theoretical considerations which suggest that Actiheart accuracy could be adversely influenced by the type of physical activity involved, the findings of the present suggest that the branched equation model equations of the Actiheart system are able to appropriately deal with physical activities involving the legs and the arms and upper torso at low to moderate levels of exercise intensity. In support of this, reasonably good correlations have been reported between Actiheart based estimates of BEE and indirect calorimetric based measures of BEE during a wide range of free living activities which included a high proportion of arm activities (Crouter *et al.*, 2008; Thompson *et al.*, 2006; Zakeri *et al.*, 2008).

### 3.4.2.2 Treadmill and Bicycle Ergometry Exercise

Studies that have compared Actiheart based estimates and indirect calorimetric measurements of BEE during treadmill walking and running have generally noted statistically high levels of agreement (Barreira *et al.*, 2009; Brage *et al.*, 2007; Corder *et al.*, 2005; Thompson *et al.*, 2006). These findings compare favorably with the close agreement between Actiheart based estimates and indirect calorimetric measurements of BEE during treadmill walking observed in the present study.

There is a paucity of studies that have directly examined the accuracy of Actiheart derived estimates of BEE during bicycle based activities at different workloads. The findings of the present study demonstrate that the Actiheart system can provide accurate BEE estimates during bicycle ergometry exercise at low to moderate exercise workloads of 150 to 600 kpm.min<sup>-1</sup>.

### 3.4.3 Critique of Methodology

#### 3.4.3.1 Accuracy of Oxycon Mobile, Treadmill and Ergometer Equipment

Indirect calorimetry is widely used to measure BEE from the rate of oxygen consumption, which in turn is calculated from measurements of minute ventilation and the difference in the inspired and expired oxygen concentrations, where  $VO_2 = V_E \times (F_{IO_2} - F_{EO_2})$  (Fox and Mathews, 1981). RER based corrections to indirect calorimetric BEE measurements were made in the present study because the amount of metabolic energy liberated per liter of oxygen consumed is dependent on the fuel being metabolised (Fox and Mathews, 1981). To further minimize errors, the Oxycon Mobile system was calibrated in accordance with the

manufacturers' instructions (Oxycon Mobile® Erich Jaeger, Viasys Healthcare, Hochberg Germany. user manual. v 5.2. 2007) immediately prior to each exercise study. However, minute ventilation and the oxygen and carbon dioxide concentrations can only be measured within a certain tolerance of accuracy, and this therefore introduced equipment based errors in the indirect calorimetric based estimates of BEE. The Oxycon Mobile manufacturer's technical specifications provide accuracies of  $\pm 2\%$  for minute ventilation,  $\pm 3\%$  for measurements of oxygen concentration and  $\pm 3\%$  for measurements of carbon dioxide concentration (Oxycon Mobile® Erich Jaeger, Viasys Healthcare, Hochberg Germany. user manual. v 5.2. 2007). In view of these considerations, there was therefore potential for significant cumulative error to occur in the indirect calorimetric based estimates of metabolic BEE. Nevertheless, the Oxycon Mobile system has been shown to provide accurate  $\text{VO}_2$  measurements over a wide  $\text{VO}_2$  range of 1 to  $5.5 \text{ L min}^{-1}$  when compared with values obtained using the traditional Douglas bag method (Rosdahl *et al.*, 2010). This conforms with similar levels of  $\text{VO}_2$  accuracy ( $\pm 2.2\%$  error) reported for nontelemetric Oxycon breath - by - breath systems compared to Douglas bag based measurements (Carter and Jeukendrup, 2002; Rietjens *et al.*, 2001).

Another potentially significant source of error in this study relates to the exercise equipment used in this study. The accuracy of the treadmill speed at the 3, 5 and  $7 \text{ km.hr}^{-1}$  settings was regularly checked by using a stopwatch to measure the time taking for the known length of the entire treadmill belt to make a full revolution with a stopwatch. The accuracy of the treadmill speeds at these settings was found to consistently remain within  $\pm 1\%$  of the measured values. The Monark 881E arm ergometer and the Monark 828E bicycle ergometer used in this study were each calibrated following the manufacturer's recommendations (Monark Ergomedic 881E manual, 2008; Monark Ergomedic 828E manual, 2008). These

calibrations were performed immediately prior to use in each participant. Steps were also taken to minimise errors resulting from moment-by-moment variations in the cadence (i.e. the number of ergometer revolutions per minute). These steps consisted of carefully instructing each participant to keep their cadence to within  $\pm 3$  rpm of the target value throughout each exercise test, and having an investigator continuously positioned near the arm or bicycle to ensure that the cadence remained within  $\pm 3$  rpm of the target value. The accuracy of the ergometer's calibration can also be affected by frictional heating. The arm and bicycle ergometers were therefore continuously monitored and the belt resistance was adjusted as required to maintain a constant mechanical workload during each exercise period.

In view of the above discussions, the available evidence suggests that methodological errors related to the Oxycon mobile, ergometers and treadmill equipment in this study were within an acceptable range and did not detract from the validity of the findings of this study.

### **3.4.3.2 Matching of Exercise Intensities for Different Exercise Modes**

In order to evaluate whether the mode of exercise affected the accuracy of the Actiheart based estimates of BEE, this study attempted to match mild to moderate exercise intensities during 3 different modes of exercise using data supplied by (Astrand and Rodahl, 1977). As shown in *Tables 3-8 to 3.10*, these attempts were successful in achieving close matching of indirect calorimetric measurements of BEE between the 3 types of exercise. This permitted the effects of the mode of exercise on Actiheart accuracy to be evaluated during essentially equivalent levels of exercise intensity.

### 3.4.3.3 Influence of RER on BEE

RER did not differ at equivalent workloads between the three modes of exercise, except for the highest workload where RER was slightly but significantly lower during bicycle ergometer exercise compared to arm ergometer or treadmill exercise (refer to **Table 3.5**). Of interest, this small disparity in RER may account for the significantly lower indirect calorimetric BEE observed at the highest bicycle workload than that seen during comparable workloads with treadmill and arm ergometer exercise (refer to **Table 3.4**), even though there was good  $\text{VO}_2$  matching between all three modes of exercise (refer to **Table 3.3**). Thus, the Actiheart system continued to accurately estimate BEE at the highest workload studied when changes in RER meant that changes in  $\text{VO}_2$  no longer precisely matched changes in BEE.

### 3.4.4 Clinical Applications

Inadequate levels of regular physical activity have been shown to be linked to a range of clinical disorders and adverse health outcomes (American College of Sports Medicine, 2011; Warburton *et al.*, 2006). Attempts to protect against the development of such disorders and adverse health outcomes by prescribing adequate levels of daily activity could be assisted by accurate and prolonged monitoring of daily activities and daily BEE. Unfortunately, technological limitations have in the past hampered accurate and prolonged BEE measurements under free living conditions. However, these limitations have been largely overcome in recent years with newly developed actigraphic systems.

Of the actigraphic systems currently available, the Actiheart system which utilizes combined heart rate and body movement sensors, provides the most reliable and accurate estimates of BEE (Corder *et al.*, 2005; Thompson *et al.*, 2006), a finding that was supported by the high accuracy of the Actiheart based BEE estimates demonstrated in the present study. Thus, the Actiheart system enables prolonged and accurate monitoring of BEE in a noninvasive and nonintrusive manner. These features open up the possibility of prolonged and accurate BEE monitoring for a range of clinical and sporting purposes in a manner that was not possible until recently, including the monitoring of existing functional disability in a range of clinical conditions.

### **3.4.5 Conclusion**

Few studies have examined the accuracy of Actiheart based estimates of BEE during common everyday daily activities that predominantly involve the arms and upper torso. Theoretical considerations such as a higher heart rate response during arm based activities suggest that the accuracy of Actiheart based BEE estimates may be influenced by the type of body movement involved in the physical activity. Therefore, the primary purpose of the current study was to examine the accuracy of Actiheart based estimates of BEE during physical activities that utilised different body movements and different muscle groups under matched mechanical workloads, and emphasis was placed on determining whether a higher heart rate response occurred during arm based exercise and whether this adversely impacted on the accuracy of Actiheart based estimates of BEE.



Actiheart based estimates of BEE between the three modes of exercise were found to be closely matched over the range of low to moderate exercise intensities examined in this study. Of particular importance, the Actiheart based estimates of BEE were also found to agree closely with simultaneous indirect calorimetric based measurements of BEE. This was evident under resting conditions and during each workload for each of the 3 types of exercise examined in this study. These findings reveal that the Actiheart system accurately estimated BEE over a range of physical activities and levels of intensity likely to be relevant to that normally encountered by people afflicted with a range of clinical disorders and functional disabilities. This was considered a prerequisite step before commencing studies that objectively examined functional disability in clinical conditions and evaluated the effects of treatment.

## Chapter 4 Actigraphic Examination of OSA Patients before and after Commencement of CPAP

### 4.1 Introduction

OSA is a serious and common disorder. The prevalence of OSA in Western countries has been estimated to be 1 to 5% in adults (Young *et al.*, 2002). The repeated periods of upper airway occlusion during sleep in OSA result in repeated episodes of hypoventilation with resultant sleep fragmentation and excessive daytime sleepiness (Malhotra and White, 2002; Remmers *et al.*, 1978; Somers *et al.*, 2008).

It is now recognised that OSA patients are less active than healthy individuals (Chasens *et al.*, 2011), are often overweight (Ali and Crowther, 2005; Young *et al.*, 2005; Young *et al.*, 1993) and are at increased risk of a range of chronic disorders and adverse health outcomes (Akahoshi *et al.*, 2010; Marin *et al.*, 2005; Nieto *et al.*, 2000; Parish and Shepard, 1990; Peppard *et al.*, 2000; Punjabi *et al.*, 2004; Silverberg *et al.*, 2002; West *et al.*, 2006). There is a large body of evidence showing that appropriate levels of daily physical activity can confer clear health benefits in a range of common clinical disorders (Hu *et al.*, 2004; Lee *et al.*, 2001; Lee and Skerrett, 2001; Lynch *et al.*, 1996; Manson *et al.*, 2002; Paffenbarger *et al.*, 1993; Sesso *et al.*, 2000; Smith *et al.*, 2000; Tanasescu *et al.*, 2002; Urata *et al.*, 1987; Warburton *et al.*, 2006). The American Heart Association and American College of Sport Medicine recommend that adults undertake at least 30 minutes of moderate intensity activity daily for at least five times a week to promote and maintain health (Haskell *et al.*, 2007). Regular exercise also plays an important role in the prevention of obesity (Bouchard *et al.*, 1993; Rippe and Hess, 1998). This is of interest because of the strong association between obesity and OSA (Ali and Crowther, 2005; Young *et al.*, 2005; Young *et al.*, 1993). In addition, many studies have demonstrated a positive correlation between excessive body

weight and a range of clinical disorders and adverse health outcomes, including OSA, hypertension, cardiovascular disease and type 2 diabetes (Ali and Crowther, 2005; Hu *et al.*, 2004; Kopelman, 2007; Wellman and Friedberg, 2002).

Nasal CPAP is the established treatment for OSA (Grunstein and Sullivan, 2000). Clinical studies have reported improvements in subjective measures of daytime sleepiness and functional outcomes relating to daily activities in OSA patients following the commencement of nightly nasal CPAP therapy (McArdle and Douglas, 2001; Montserrat *et al.*, 2001; Patel *et al.*, 2003). Chasens *et al.* (2011) have argued that excessive daytime sleepiness may play a role in decreased functional activities in OSA patients. However, this possibility does not appear to have been investigated to date, and ideally would involve objective quantification of daily activities.

Technical limitations have prevented making sustained objective measurements of daily activities in the past. Indeed, only one recent study by Chasens *et al.* (2011) has attempted to objectively quantify daily activity in OSA patients with a two-axial accelerometer Bodymedia SenseWear Pro Armband and compare these data with self-reporting scores of daily activity. Although the study by Chasens *et al.* (2011) failed to find a correlation between subjective and objective measures of daily activity (FOSQ versus BodyMedia Armband measures of daily steps taken and estimated energy expenditure), a number of studies have reported poor accuracy with Bodymedia Armband based estimates of energy expenditure (Berntsen *et al.*, 2010; Bertoli *et al.*, 2008; Papazoglou *et al.*, 2006; Soric *et al.*, 2012). In contrast, advances in actigraphic technology have recently led to the commercial release of small portable equipment such as the Actiheart system which has been well validated and with which it is now possible to accurately estimate daily BEE over prolonged periods of time.

Until recently, technical limitations have precluded making continuous prolonged measurements of BEE under free living conditions. Consequently, little is known concerning the profile of daily BEE in either healthy or diseased free living individuals. The Actiheart's ability to accurately and continuously estimate and digitally record daily BEE over prolonged periods of time (days or weeks) has provided a unique opportunity to address this deficiency. However, for prolonged measurements, the Actiheart system currently only provides estimates of energy expenditure that are related to physical activity (AEE which equals total BEE minus resting BEE) during long term recordings. Thus, the Actiheart system can provide not only accurate estimates of daily AEE, but with suitable computerised data handling procedures, can also quantitatively map out how AEE varies from minute-to-minute over entire 24 hour periods in OSA patients before and after commencement of nightly CPAP therapy.

#### **4.1.1 Aim of the Study**

In view of the above mentioned considerations, a novel study was carried out with OSA patients to determine for the first time:

1. Whether subjective measures of daily activity correlated with objective measures of daily BEE made with the well validated Actiheart system.
2. Whether improvements in daytime sleepiness resulting from nightly CPAP therapy correlated with improvements in objective and subjective measures of daily activity.
3. How AEE varies from minute-to-minute over entire 24 hour periods, and how such daily BEE profiles are affected by nightly CPAP therapy.

## 4.2 Materials and Methods

This study was approved by the University of New England Human Research Ethics Committee (Approval No. HE12/101, Valid to 30/11/2014), and each participant gave informed consent prior to commencement of the study. Each participant was carefully instructed regarding the details of the study and that he was free to withdraw from the study at any time.

### 4.2.1 Participants

All participants in this study were men aged over 18 years with recently diagnosed OSA, and were excluded from the study if they had significant comorbidities that could impair physical mobility. A total of 32 men who had recently been diagnosed with OSA were initially recruited into this study prior to them commencing nightly treatment with nasal CPAP. However, 20 of these men subsequently withdrew from the study either because of minor skin irritation from the Actiheart system's ECG electrodes (n=6), or because they were not available for one or more of the measurement periods within the designated study period (n=14). Data from the remaining 12 OSA patients are reported in this study.

Each of the 12 participants had been diagnosed as having OSA following overnight polysomnography at the Armidale Private Hospital's Respiratory Failure and Sleep Disorders Unit. An apnoea-hypopnoea index of  $\geq 5$  significant respiratory-related reductions in breathing (apnoeas and hypopnoeas) per hour was taken as the diagnostic criteria of OSA (ASTA/ASA, 2010; Australasian Sleep Association, 2014), where apnoeas were defined as a complete cessation of airflow related with a  $\geq 4\%$  decrease in oxygen saturation that persisted for  $> 10$  seconds, and

hypopnoeas were defined as at least a 30% decrease in airflow related with a drop of at least 4% in oxygen saturation that persisted for > 10 seconds.

## **4.2.2 Measurements**

### **4.2.2.1 Anthropometric Characteristics**

Each participant's body weight was measured to the nearest tenth of a kilogram with scales (Omron Healthcare Co. Ltd, Japan, model HBF-500) while they wore light clothing without shoes. Height was measured to the nearest 0.5 cm with a standard stadiometer while the participant stood erect without shoes. Body weight and height measurements were then used to calculate the BMI using the following equation:

$$\text{BMI (kg.m}^{-2}\text{)} = \text{Body mass (kg)} \div \text{Height}^2 \text{ (m}^2\text{)}.$$

### **4.2.2.2 Psychometric Scoring of Subjective Measurements**

#### **4.2.2.2.1 Daytime Sleepiness**

Subjective daytime sleepiness was assessed over each of the three one week long study periods with the Epworth Sleepiness Scale (ESS) which consists of an 8 item self-reporting questionnaire (Johns, 1993). Each of the eight items addresses a different aspect relating to daily life, and participants semi-quantitatively rated their response to each item using a four point Likert scale that ranged from 0 (no chance of dozing) up to 3 (high chance of dozing) during the week study. The total cumulative score on the ESS out of a maximum possible score of 24 was then calculated and used as a subjective index of daytime sleepiness.

#### 4.2.2.2 Functional Activity

The Functional Outcomes of Sleep Questionnaire (FOSQ-30) (Weaver *et al.*, 1997) was used to assess the functional daily activities that occurred over week long periods. The FOSQ-30 was designed to assess the impact of sleepiness on daily life activities and consists of 30 self-reporting questions that address five different domains relating to daily life activities - Activity levels (9 questions), Vigilance (7 questions), Intimacy and sexual relationships (4 questions), General productivity (8 questions) and Social outcome (2 questions). Participants semi-quantitatively rated their response to each question using a five point Likert scale that ranged from 0 to 4, with high scores signifying a low adverse impact on daily living activities. The cumulative scores were then calculated for each domain on the FOSQ-30, averaged and multiplied by 5 to give a maximum possible score of 20 for each domain. The total FOSQ-30 score was then calculated as cumulative score from all 5 domains giving a maximum possible score of 100, and was used as a semi-quantitative subjective index of the extent to which daytime sleepiness had affected daily living activities over the past week.

#### 4.2.2.3 Actigraphic Measurements of Daily Activity

AEE was estimated with an Actiheart system (Actiheart 4, AH4, CamNtech Neurotechnology Ltd, Cambridge UK) which was positioned over the participant's chest as previously described in **section 2.2.3.1 *Equipment calibration and participant instrumentation***. Participants were instructed to wear the Actiheart system during the study period except when showering or bathing. For each participant, minute-by-minute estimates of AEE were made over entire days for one week periods.

At the end of each recording week, heart rate and 3 dimensional body movement data recorded with the Actiheart system were transferred onto a lap top computer using an Actiheart reader system (CamNtech Neurotechnology Ltd, Cambridge UK, serial no 320208). Actiheart system software (CamNtech Neurotechnology Ltd, Cambridge UK. software v.4.0.89) was used to analyse the recorded Actiheart data over 60 second epochs. The captured data was then analysed with a validated branched-equation model (Brage *et al.*, 2007) which have also been previously discussed in detail (refer to *section 2.2.4 Data Analysis*).

#### **4.2.2.4 Experimental Protocol**

AEE data was continuously recorded for 3 separate 7 day periods, except for short daily periods during bathing or showering. These 3 one week long periods occurred 1-2 weeks prior to the commencement of nightly CPAP treatment (Pre-CPAP), 1-2 weeks after the commencement of nightly CPAP treatment (CPAP-1), and 5-6 weeks after the start of nightly CPAP treatment (CPAP-2). Each participant also completed the ESS and FOSQ-30 at the end of each of the 3 Actiheart recording weeks.



#### 4.2.2.5 Data Analysis

##### 4.2.2.5.1 Analysis of Actiheart Data

Computer generated minute-by-minute actigraphic estimates of AEE over entire one week long periods were downloaded into an Excel (Computer Software, Washington, USA. Microsoft v. 14.0, 2010) spreadsheet, and summated to give the entire AEE expended over the week long period. This value was then divided by 7 to determine the average daily AEE ( $\text{kJ}\cdot\text{day}^{-1}$ ). This analysis was carried out separately for each of the 3 one week long actigraphic measurement periods in each participant.

Excel spreadsheets containing minute-by-minute actigraphic AEE estimates made over entire one week long periods were further analysed to examine the percentage of time spent at various levels of AEE. These analyses were graphically illustrated both as pie graphs and as histograms. The levels of AEE chosen for the pie graphs were: 0-1.99 (no to light physical activities), 2.00-5.00 (moderate physical activities) and  $> 5.00$  (vigorous physical activities) metabolic equivalents (METs). These values were modified from the total BEE classification used by Haskell *et al.* (2007), where one MET is taken to be the standard adult resting metabolic rate of  $4.184 \text{ kJ}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$  (Ainsworth *et al.*, 2000), so that AEE equals total body expenditure minus 1.00 METs (Thompson *et al.*, 2006). Histograms were generated in Excel spreadsheets using 0.01 MET AEE increment ranging from 0 to 5.00 METs. A separate pie graph and histogram was generated for each of the 3 week long actigraphic measurement periods in each participant. In addition, an averaged pie graph and histogram was also generated for the 12 participants for each of the 3 week long study periods.

#### 4.2.2.5.2 Statistical Analysis

Unless otherwise stated, all data were expressed as means  $\pm$  1 standard deviation. Data were analysed to test for normal distribution using Kolmogorov-Smirnov and Shapiro-Wilk tests (Peat and Barton, 2008). Serial measurements of normally distributed data were statistically analysed using one-way ANOVAs and *post-hoc* Tukey's tests (null hypothesis rejected at  $P < 0.05$ ) to determine whether there were significant differences between the mean data obtained from Pre-CPAP, CPAP-1 and CPAP-2 (Dowdy *et al.*, 2003). Serial measurements of data that were not normally distributed were statistically analysed using Wilcoxon signed ranks tests with Bonferroni adjustments to accommodate 3 comparisons (null hypothesis rejected at  $P < 0.0167$ ) (Dowdy *et al.*, 2003; Utts and Heckard, 2005). Statistical analysis of the data was performed with SPSS software (IBM Corp, Amonk, NY, USA. *SPSS Statistic for windows v. 19.0.* 2010). The null hypothesis was rejected at  $p < 0.05$ .

### 4.3 Results

No adverse effects were noted in this study other than a mild but persistent skin irritation on the anterior chest surface which resulted from ongoing exposure to the adhesive strips attached to the Actiheart ECG electrodes in 6 potential participants who were excluded from the study.

The anthropometric characteristics of the 12 OSA patients who completed the study are provided in *Table 4-1*. At the commencement of the study, each of the 12 participants had a BMI  $\geq 26 \text{ kg.m}^{-2}$ , and 75% of the participants were obese with BMI  $\geq 30 \text{ kg.m}^{-2}$  (World Health Organization, 2000). The apnoea - hypopnoea index prior to the commencement of nightly CPAP therapy was  $33.2 \pm 10.9$  (range from 9.2 to 46.9) apnoeas and hypopnoeas per hour of sleep. In addition, at the commencement of the study each of the 12 OSA patients had an ESS  $> 5$ , and 7 (58%) of the 12 OSA patients had excessive daytime sleepiness with an ESS  $> 10$ .

*Table 4-1:* Anthropometric characteristics of 12 men recently diagnosed with OSA.

Age (years)	45.3 $\pm$ 14.3
Body mass (kg)	105 $\pm$ 16
Height (cm)	179 $\pm$ 5
BMI ( $\text{kg.m}^{-2}$ )	32.5 $\pm$ 4.2

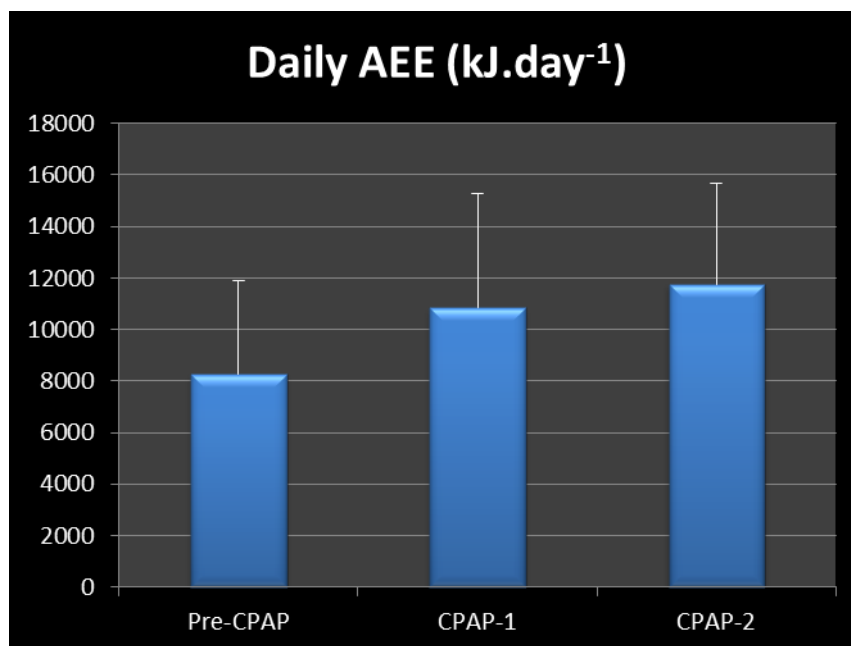
FOSQ data (FOSQ-30 and each of its 5 domains) were normally distributed, but ESS data was not. The responses of daily AEE, ESS, and FOSQ-30 and its 5 domains to nightly CPAP therapy are shown in **Table 4-2** and **Figures 4.1** to **4.8**. Daily AEE data increased after 4-6 weeks of CPAP, but not after 1-2 weeks of CPAP. The ESS and FOSQ-30 both improved significantly after 1-2 weeks of CPAP, but further significant improvements were only evident in ESS after 4-6 weeks of CPAP. Four of the 5 FOSQ domains (Activity, Vigilance, Intimacy and General productivity) increased significantly after 1-2 weeks of nightly CPAP therapy, but although these 4 FOSQ domains remained significantly elevated relative to Pre-CPAP levels after 4-6 weeks of CPAP, there were no further increases after 1-2 weeks of CPAP.

**Table 4-2:** Daily AEE (kJ.day<sup>-1</sup>), ESS, FOSQ-30, and FOSQ domains at Pre-CPAP, CPAP-1 and CPAP-2. for 12 OSA participants.

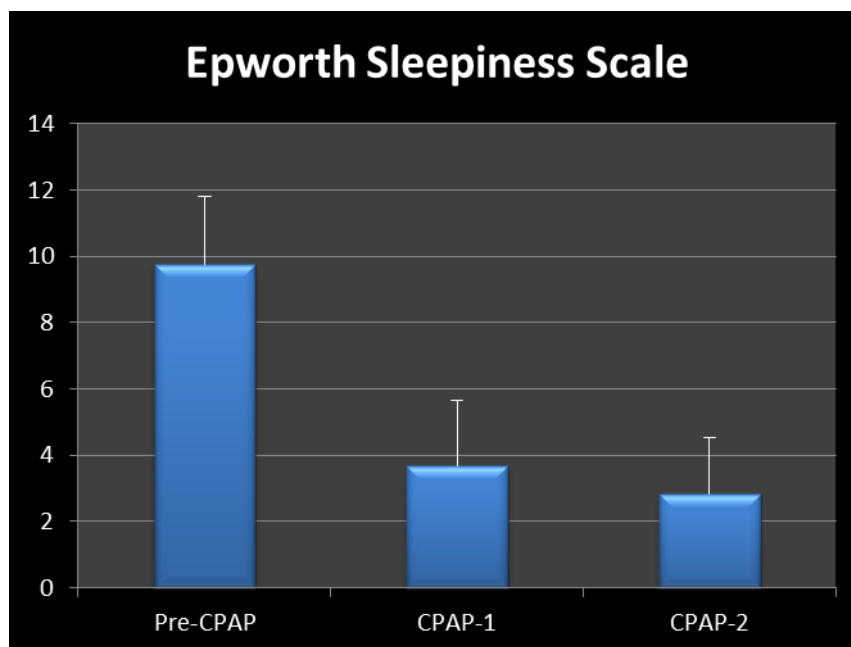
Variable	Pre-CPAP	CPAP-1	CPAP-2
AEE (kJ.day <sup>-1</sup> )	8,265 ± 3,610	10,842 ± 4,430	11,766 ± 3,912*
ESS	9.75 ± 2.05	3.67 ± 1.97§	2.83 ± 1.70 †*
FOSQ-30	79.1 ± 8.5	91.8 ± 4.9§	96.3 ± 2.3*
FOSQ-Activity	15.3 ± 1.7	17.8 ± 1.5§	18.8 ± 0.7*
FOSQ-Vigilance	14.8 ± 2.6	18.2 ± 1.7§	19.2 ± 0.9*
FOSQ-Intimacy	16.1 ± 3.1	18.2 ± 1.5§	19.1 ± 1.3*
FOSQ-General productivity	15.2 ± 2.8	18.4 ± 1.1§	19.3 ± 0.7*
FOSQ-Social outcome	18.6 ± 1.7	19.6 ± 1.0	19.8 ± 0.7

§  $p < 0.05$  relative to Pre-CPAP, †  $p < 0.05$  relative to CPAP-1, \*  $p < 0.05$  relative to Pre-CPAP.

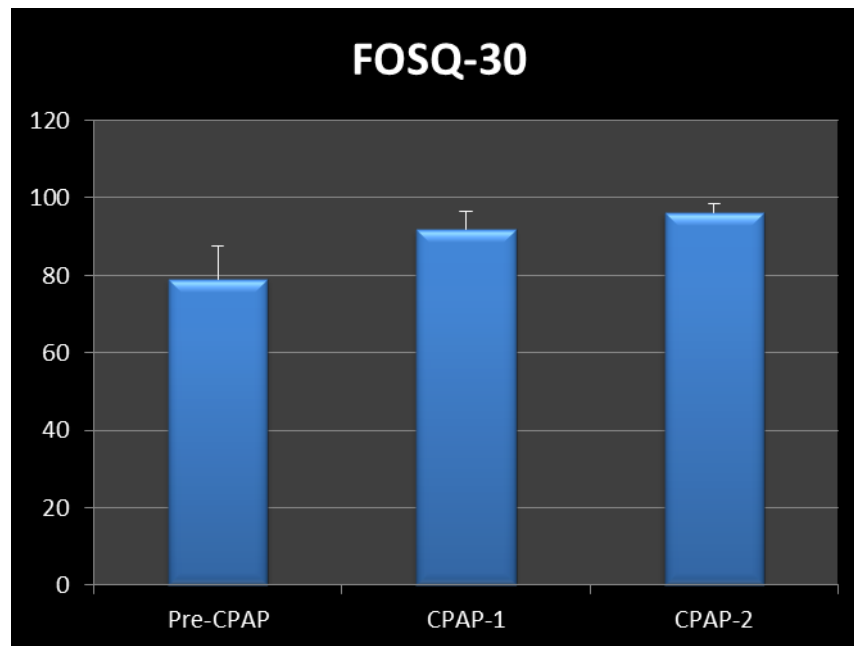
**Figure 4-1:** Daily AEE ( $\text{kJ}\cdot\text{day}^{-1}$ ) measurements at Pre-CPAP, CPAP-1 and CPAP-2. Data are means  $\pm$  SD for 12 men with OSA.



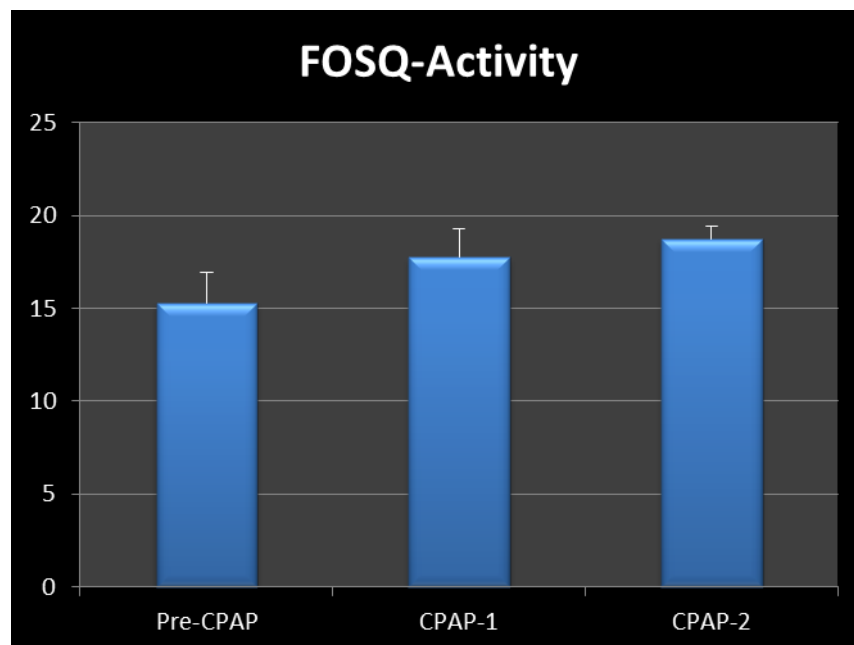
**Figure 4-2:** ESS at Pre-CPAP, CPAP-1 and CPAP-2. Data are means  $\pm$  SD for 12 men with OSA.



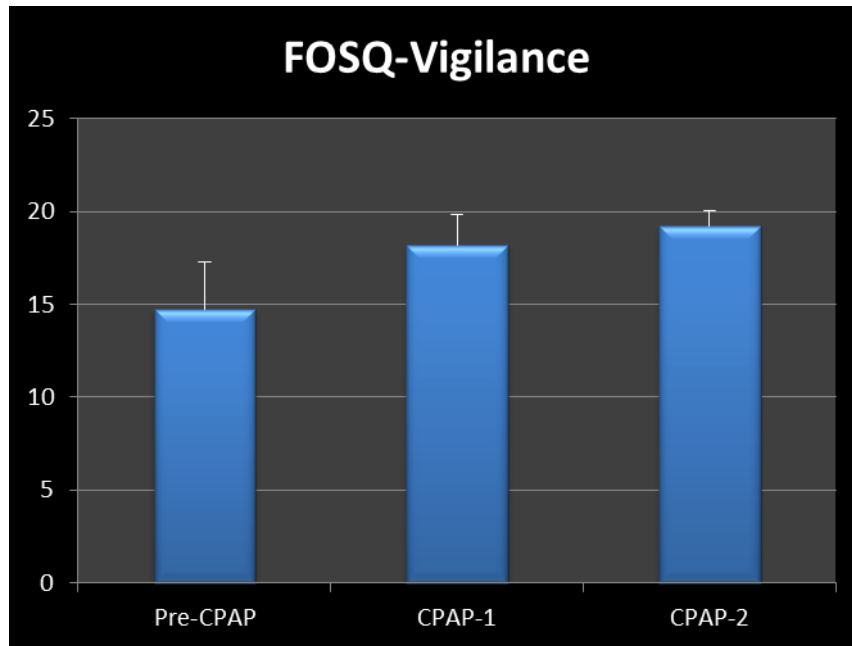
**Figure 4-3:** FOSQ-30 at Pre-CPAP, CPAP-1 and CPAP-2. Data are means  $\pm$  SD for 12 men with OSA.



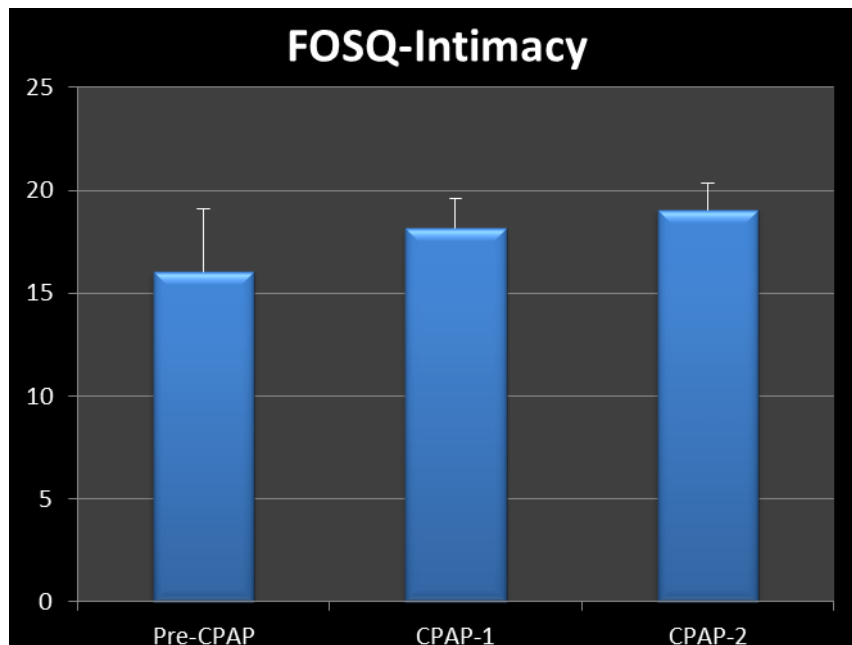
**Figure 4-4:** FOSQ-Activity at Pre-CPAP, CPAP-1 and CPAP-2. Data are means  $\pm$  SD for 12 men with OSA.



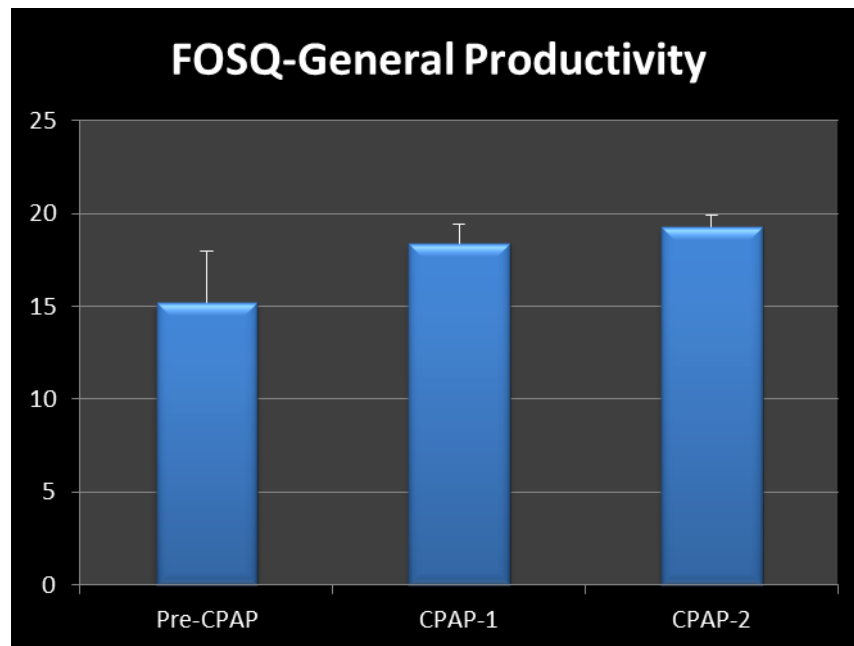
**Figure 4-5:** FOSQ-Vigilance at Pre-CPAP, CPAP-1 and CPAP-2. Data are means  $\pm$  SD for 12 men with OSA.



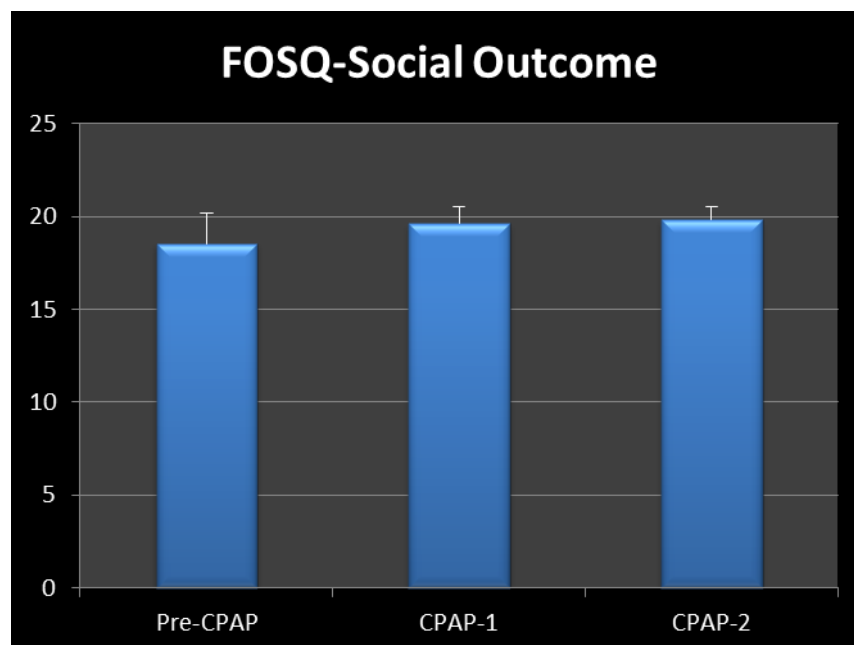
**Figure 4-6:** FOSQ-Intimacy at Pre-CPAP, CPAP-1 and CPAP-2. Data are means  $\pm$  SD for 12 men with OSA.



**Figure 4-7:** FOSQ-General productivity at Pre-CPAP, CPAP-1 and CPAP-2. Data are means  $\pm$  SD for 12 men with OSA.



**Figure 4-8:** FOSQ-Social outcome at Pre-CPAP, CPAP-1 and CPAP-2. Data are means  $\pm$  SD for 12 men with OSA.

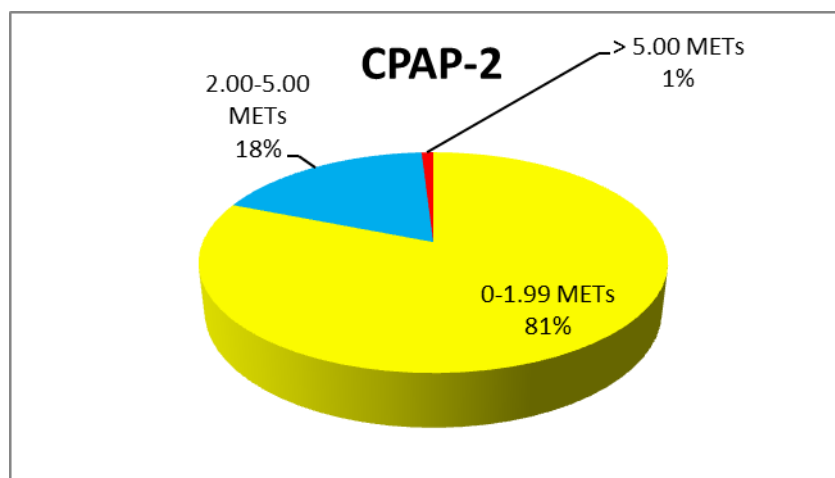
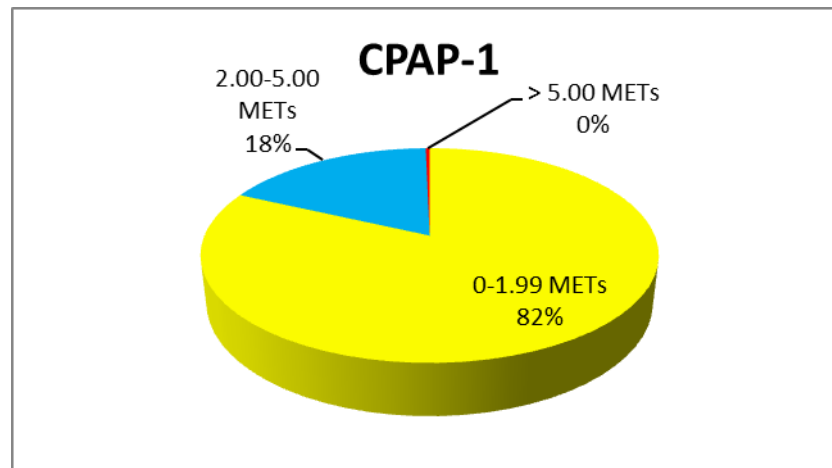
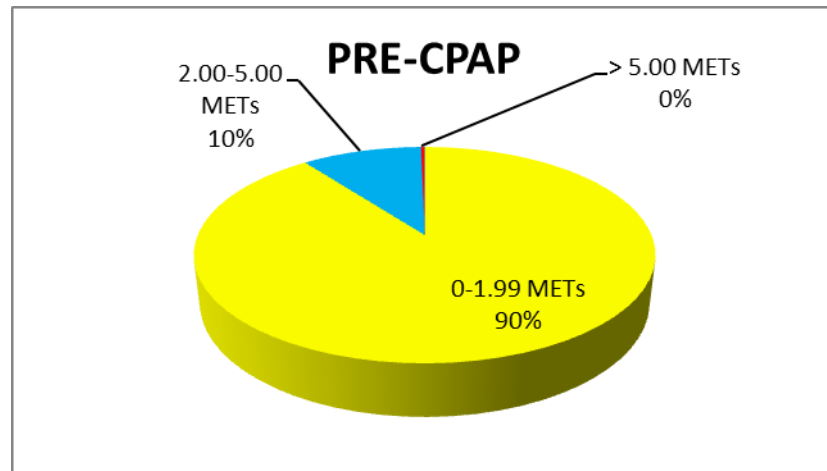




The average percentage of total time spent at different levels of AEE over the three 1 week actigraphic recording periods for the 12 OSA patients is shown in **Table 4.3** and depicted as pie diagrams in **Figure 4.9**. The average frequency distribution of AEE for the 12 OSA patients is depicted in **Figure 4.10**. Individual pie diagrams and individual frequency distribution diagrams for each of the 12 OSA patients are provided in **Appendix 1** and **Appendix 2** respectively. Although AEE reached as high as 15.85 METs during a single one minute recording epoch in one OSA patient, AEE rarely exceeded 5.00 METs in this study. Consequently, the histograms depicted in **Figure 4.10** were generated using 0.01 MET AEE increments ranging from 0.00 to 5.00 METs. The percentage of total time spent at different levels of AEE over the three 1 week long actigraphic recording periods was normally distributed for the 0 to 1.99 and > 5.00 METs data.

The amount of time spent at the lowest MET level (0 to 1.99 METs) decreased after commencement of nightly CPAP, with a concomitant increase in the amount of time spent at 2.00 to 5.00 METs. The numeric decrease in the percentage of total time spent at 0 to 1.99 METs from Pre-CPAP to CPAP-1 almost reached statistical significance ( $p = 0.052$ ), and fell significantly from Pre-CPAP to CPAP-2 (refer to **Table 4.3**). Concomitantly, the percentage of total time spent at 2.00 to 5.00 METs increased significantly from Pre-CPAP to CPAP-1 and from Pre-CPAP to CPAP-2. Although, small numeric increases were observed in the percentage of total time spent at > 5.00 METs after the commencement of nightly CPAP, these did not reach statistical significance. Visual comparison of the average daily AEE histograms for the group revealed a large numeric decrease in the amount of time spent at 0-0.1 METs after commencement of nightly CPAP therapy, and a small sustained increase in the amount of time spent at approximately 1.4 to 3.2 METs. This effect was already evident at CPAP-1. Body weight did not change during the study ( $105 \pm 16$  kg at Pre-CPAP,  $105 \pm 16$  kg at CPAP-1 and  $103 \pm 16$  kg at CPAP-2 (all  $P = 0.99$  relative to pre-CPAP)).

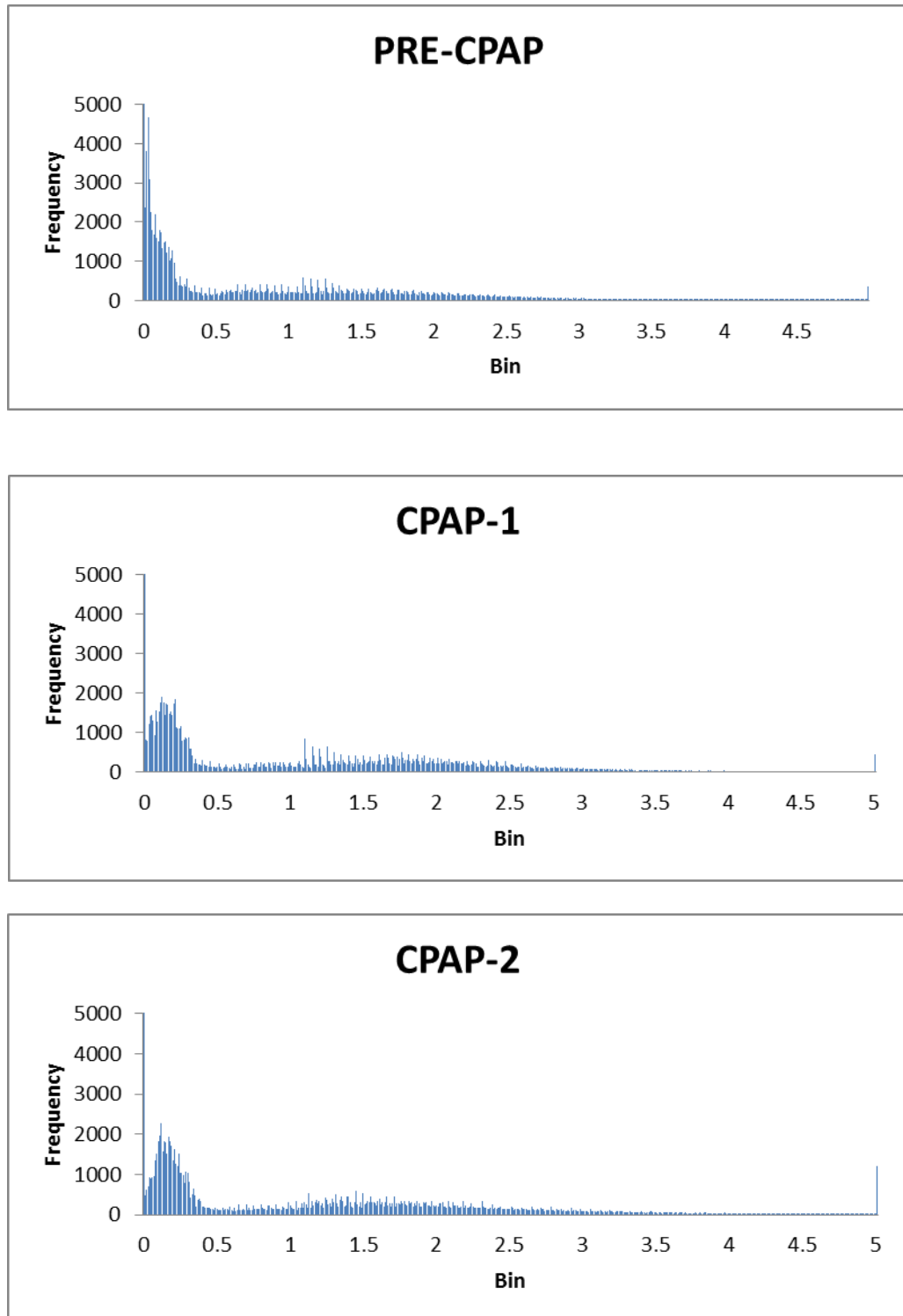
**Figure 4-9:** Percentage of total time spent at different levels of AEE over the three 1 week actigraphic recording periods (Pre-CPAP, CPAP-1 and CPAP-2). Data are mean values from 12 male OSA patients.



**Table 4-3:** Percentage of total time spent at different levels of AEE over the three 1 week actigraphic recording periods (Pre-CPAP, CPAP-1 and CPAP-2). Data are means  $\pm$  SD from 12 OSA patients. \*  $p < 0.05$  relative to Pre-CPAP, §  $p < 0.05$  relative to Pre-CPAP. There were no significant differences between CPAP-1 and CPAP-2.

<b>Level of AEE</b>	<b>Pre-CPAP</b>	<b>CPAP-1</b>	<b>CPAP-2</b>
0.00-1.99 METs	89.6 $\pm$ 0.6%	81.9 $\pm$ 0.6%	81.1 $\pm$ 1.9% *
2.00-5.00 METs	10.0 $\pm$ 0.7%	17.8 $\pm$ 0.6% §	18.0 $\pm$ 1.7% *
> 5.00 METs	0.3 $\pm$ 0.7%	0.3 $\pm$ 0.7%	1.0 $\pm$ 2.0%

**Figure 4-10:** Histogram showing the number of minutes (frequency) that 12 participants spent at different levels of AEE during the three 1 week study periods. AEE is depicted on the X axis in 0.1 MET increments ranging from 0.00 to 5.00 METs. Top panel depicts data collected during the Pre-CPAP period. Middle panel depicts data collected during the CPAP-1 period. Bottom panel depicts data collected during the CPAP-2 period.



## 4.4 Discussion

This is the first study to examine the effects of nightly CPAP therapy on functional activities in OSA patients using both objective and subjective measurements of daily activity. Daily AEE, ESS, FOSQ-30 and its 5 domains (except FOSQ-Social outcome) each improved significantly at CPAP-2 relative to Pre-CPAP levels. In addition, the amount of time spent daily at the lowest AEE of 0-1.99 METs fell significantly from Pre-CPAP to CPAP-2, and this corresponded with a decrease in the amount of time spent at an AEE of 2.00-5.00 METs. Thus, the improvements in the subjective measure of daily activity (FOSQ-30 and 4 of its 5 domains) at CPAP-2 occurred concurrently with an increased daily AEE, a decrease in the amount of time spent daily at an AEE of 0-1.99 METs and an increase in the amount of time spent daily at an AEE of 2.00-5.00 METs. Statistically significant improvements in the FOSQ-30 and 4 of the 5 FOSQ domains were evident after only 1-2 weeks of nightly CPAP therapy. In contrast, statistically significant changes in daily AEE were not evident after only 1-2 weeks of nightly CPAP therapy. It therefore took longer for statistically significant changes to become evident in daily AEE compared to that observed in the FOSQ-30 and its domains. Improvements in daytime sleepiness also occurred concurrently with improvements in the subjective measure of daily activity at both CPAP-1 and CPAP-2, so that the increases in daily AEE also lagged behind the improvements seen in the ESS.

#### 4.4.1 Relationship Between Daytime Sleepiness and Functional Outcomes

Chasens *et al.* (2011) have argued that excessive daytime sleepiness may play a role in decreased functional activities in OSA patients. In support of this, good inverse correlations between the ESS and FOSQ have been reported in OSA patients (Chasens *et al.*, 2011; Weaver *et al.*, 2007). Potentially, a reduction in excessive daytime sleepiness from CPAP therapy could lead to improved functional activities and associated health benefits in OSA patients. However, no detailed investigation into this possibility has yet been reported in the literature.

The improvements in ESS and FOSQ with CPAP observed in the present study are consistent with the findings of previous studies (McArdle and Douglas, 2001; Montserrat *et al.*, 2001; Patel *et al.*, 2003). In addition, the improvements in ESS mirrored the improvements seen in the FOSQ-30 which is consistent with previous studies that have shown good inverse correlation between these psychometric measures in OSA patients (Chasens *et al.*, 2011; Weaver *et al.*, 2007). However, unlike most previous studies, these psychometric measures were made at two times after the commencement of nightly CPAP therapy in the present study, CPAP-1 (1-2 weeks of CPAP) and CPAP-2 (4-6 weeks CPAP), and improvements in the ESS occurred concurrently with improvements in the FOSQ-30 and its domains at both study periods.

The Actiheart system used in this study not only enabled AEE to be objectively measured in  $\text{kJ}\cdot\text{day}^{-1}$ , but also provided daily AEE profiles which quantified the amount of time spent daily at different levels of AEE. Thus, this study can report for the first time that 4-6 weeks of nightly CPAP therapy in a group of OSA patients was associated with an average increase in daily AEE of 3,501 kJ, an 8.5% decrease in the amount of time spent daily (2.0 hours) at an AEE of 0-1.99 METs and an 8% increase in the amount of time spent per day (1.9 hours) at an AEE of 2.00-5.00

METs. Daily AEE profiles depicted as histograms revealed a preponderance of time spent at low levels of activity which is consistent with a sedentary lifestyle. This supports the view by Chasens *et al.* (2011) that OSA patients are less active than healthy individuals. The author is not aware of any published daily BEE histograms from healthy individuals or patients, and the extent to which the daily AEE histograms from the OSA patients of the present study differ from that of healthy individuals therefore cannot be resolved at this time. However, visual comparison of the daily AEE histograms revealed a large numeric decrease in the amount of time spent at 0-0.1 METs after commencement of nightly CPAP therapy, and a small sustained increase in the amount of time spent at approximately 1.4 to 3.2 METs. This effect was already evident at CPAP-1.

Significant changes in daily AEE only became evident after 4-6 weeks of nightly CPAP therapy, whereas significant improvements were already evident in the ESS, FOSQ-30 and its domains after 1-2 weeks of CPAP. Other studies have commented on disparities between subjective and objective measures of sleepiness (Weaver *et al.*, 2007) and subjective and objective measures of daily activities (Baptista *et al.*, 2012; Blair *et al.*, 2001; Chasens *et al.*, 2011), with subjective measurements of daily activities typically exceeding objective measurements (Baptista *et al.*, 2012). It has been argued that this disparity may reflect subjective bias in the case of sleepiness (Weaver *et al.*, 2007) and daily activities (Baptista *et al.*, 2012). Chasens *et al.* (2011) reasoned that subjective instruments measure subjective difficulty which is distinct from objective behaviour. Of interest, Chasens *et al.* (2011) used an armband two-axial accelerometer (Bodymedia SenseWear Pro Armband) to objectively quantify daily activities, and were unable to detect a correlation with this measure and the FOSQ-30 in a group of OSA patients. However, the Bodymedia SenseWear Pro Armband does not accurately measure BEE at rest (Bertoli *et al.*, 2008) or during various physical activities (Berntsen *et al.*, 2010; Soric *et al.*, 2012). This

limitation may account for the lack of association between objective and subjective measures of daily activities in the study by Chasens *et al.* (2011).

Overall, the findings of this study support the view by Chasens *et al.* (2011) that excessive daytime sleepiness may play a role in decreased functional activities in OSA patients. Theoretically, the delayed increase in daily AEE and the delayed decrease in the amount of time spent daily at an AEE of 0-1.99 METs, compared with the more rapid improvements in the subjective measures of sleepiness and functional activities, may reflect a slower onset of behavioural changes in daily activities when excessive daytime sleepiness is reduced. This possibility serves to illustrate the potential benefits of including actigraphic estimates of daily AEE to provide more comprehensive monitoring of functional outcomes in OSA patients receiving CPAP therapy.

## **4.4.2 Critique of Methodology**

### **4.4.2.1 Protocol Considerations**

A number of factors relating to the duration of the measurement periods were considered when designing this study. Berlin *et al.* (2006) reviewed the relevant literature and noted that accelerometer based measurements needed to be carried out for 4 to 12 days in order to obtain consistent and representative measurements of daily activities. A primary consideration when attempting to obtain representative measurements of daily activities was to ensure that daily fluctuations over the weekly cycle (e.g. more leisure time on weekends) were taken into account (Tudor-Locke *et al.*, 2004). In view of these considerations, it was decided to continuously record AEE for entire one week long periods, and to have each of the patients complete the ESS and FOSQ-30 self-reporting questionnaires at the end of each of the week long AEE recording



periods. As an additional consideration, the experimental protocol was designed so that measurements were repeated at both 1-2 weeks and 4-6 weeks after commencement of nightly CPAP therapy in order to ensure that an adequate duration of CPAP treatment was given and to examine and compare the time course of different CPAP-related improvements. This experimental design proved useful in identifying a time lag between increased AEE and improvements in the ESS and FOSQ.

#### **4.4.2.2 Validity of Data from Self-reporting Questionnaires**

Well validated techniques were used to quantify sleepiness and daily activities in this study. The ESS was used in this study to measure daytime sleepiness. It is a self-reporting questionnaire that has been well validated and has been widely used in many OSA studies (Johns, 2000; Jons, 1993; Weaver *et al.*, 2007). The FOSQ-30 was used in this study to provide a subjective means of evaluating functional activities. It is a well validated self-reporting questionnaire that was specifically designed to examine the effects of sleepiness on daily activities and has been widely used for this purpose in many OSA studies (Chasens *et al.*, 2011; Weaver *et al.*, 1997).

#### **4.4.2.3 Validity of Actiheart AEE Estimates**

The Actiheart system which was used to measure BEE in this study has been well validated and has been shown to give accurate BEE estimates over a wide range of physical activities in healthy participants (Barriera *et al.*, 2009; Crouter *et al.*, 2008; Thompson *et al.*, 2006; Zakeri *et al.*, 2008), although little is known about its accuracy in patients with significant disorders. Moreover, as discussed in detail in section *1.1.7 Estimation of Body Energy*

*Expenditure from Combined Heart Rate and Accelerometer Monitoring*, the Actiheart system appears to be the best currently available device for actigraphically estimating AEE.

Although the Actiheart has been well validated over a wide range of physical activities, and strong correlations between Actiheart based estimates of BEE and indirect calorimetric measurements of BEE have been demonstrated during physical activities ranging from low to moderate intensity (Barriera *et al.*, 2009; Crouter *et al.*, 2008; Thompson *et al.*, 2006; Zakeri *et al.*, 2008), the Actiheart has not been mathematically modelled or validated for very low levels of  $AEE < 1$  MET. However, no evidence of a fixed or relative bias in Actiheart estimates of total BEE was observed at low exercise intensities in the first study in this thesis. Indeed, the regression lines for the Actiheart BEE versus Oxycom BEE plots essentially passed through the origin (0, 0) (refer to *Figures 2.4* and *2.5*), implying that the high level of correlation between simultaneous Actiheart BEE and Oxycom BEE values continued down to zero levels of BEE. The experimental protocol in the present study allowed participants to disconnect from the Actiheart for short daily periods during bathing or showering, and this would have had a small but unquantifiable effect on the AEE data.

#### **4.4.2.4 Daily AEE Profiles**

The Actiheart's ability to accurately and continuously estimate and digitally record daily AEE on a minute-by-minute basis over prolonged periods of time (days or weeks) provided a unique opportunity to quantitatively map out how AEE varied over entire one week periods in OSA patients before and after commencement of nightly CPAP therapy. The analysis of daily AEE profiles was carried out by calculating the percentage of the entire week long recording

periods that the OSA participants spent at different levels of AEE, and by generating histograms that depicted the amount of time spent at different levels of AEE in 0.1 MET increments. To the author's knowledge this is the first time that such detailed and objective analysis of daily activities has been reported under free living conditions in either healthy participants or patients.

There is extensive literature on the estimated MET levels for different types and intensities of activities of daily living (Ainsworth *et al.*, 2000; American College of Sports Medicine, 2011; Bassett *et al.*, 2000; Haskell *et al.*, 2007). Admittedly, these MET levels are only indirect estimates of total BEE and can fail to take into account individual differences (Ainsworth *et al.*, 2000). Nevertheless, it was considered useful to express the daily AEE profiles in the present study in METs because this could potentially allow inferences to be made regarding how much time was spent at levels of AEE that roughly corresponded to different common daily activities, and to examine whether this changed after commencement of nightly CPAP therapy.

The MET ranges chosen for AEE in this study were based on the total BEE classification of physical activities intensity reported by Haskell *et al.* (2007). However, AEE equals the total BEE in METs minus the standard resting metabolic rate of 1.00 METs (Thompson *et al.*, 2006). Therefore, to take into account the contribution made by the resting metabolic rate to the total body energy expenditure, the AEE MET ranges used in the present study were calculated as the total BEE MET ranges from the report by Haskell *et al.* (2007) minus 1.00 METS.

Sleep was an important consideration in the present study. However, it was not possible to determine a clear cut off in METs which consistently identified when the OSA patients in the present study were sleeping. Several factors contributed to this limitation. First, there is debate about what constitutes the true resting metabolic rate and the MET level during sleep. Total BEE

during sleep is widely taken as equaling 0.9 METs which is 0.1 METs lower than the standard resting metabolic rate of 1.0 METs (Ainsworth *et al.*, 2000). However, Byrne *et al.* (2005) have argued that a MET of 1.0 overestimates the true resting metabolic rate by 20%. Second, Actiheart estimates of AEE will remain at 0 METs in a fully resting individual regardless of whether s/he is asleep or awake, and this hampers the use of Actiheart based estimates of AEE to distinguish between the two states. Thirdly, distinguishing between sleep and awake resting conditions is likely to be further complicated by fluctuations in AEE during sleep. heart rate undergoes cyclical variation between apneas/hypopnoeas and the resumption of breathing in sleeping OSA patients (Guilleminault *et al.*, 1984), and periodic limb movements are common during sleep in OSA patients (Baran *et al.*, 2003; Carelli *et al.*, 1999; Fry *et al.*, 1989; Hedli *et al.*, 2012). Such movements can involve not only the legs, but also the upper extremities (Chabli *et al.*, 2000) and the abdominal muscles (Seo and Guilleminault, 2012). The Actiheart system estimates AEE using ECG derived heart rate inputs and accelerometer derived body movement inputs (Brage *et al.*, 2007; Thompson *et al.*, 2006), so that periods of fluctuating heart rate and body movements register as fluctuations in AEE during sleep.

Unlike the study by Haskell *et al.* (2007), sleep was an important consideration in the present study. However, because of the inability to actigraphically determine when the OSA patients were sleeping, the lowest MET range in the report by Haskell *et al.* (2007) was modified to incorporate both sleep and light activities. The extensive compendium of estimated MET levels for different physical activities published by Ainsworth *et al.* (2000) lists light activities within this low intensity MET range as those involving sitting or standing with little activity.

### 4.4.3 CPAP Related Changes in the Daily AEE Profile

The extensive list of estimated MET levels for different physical activities compiled by Ainsworth *et al.* (2000) lists the AEE range of 0-1.99 as corresponding to sleeping or sitting/standing with little activity, while an AEE range of 2.00-5.00 METs corresponds to activities that involve body movement with moderate but not vigorous exertion. The 8.5 % CPAP related reduction in the amount of time spent at an AEE of 0-1.99 METs and the concomitant 8.0% increase in the amount of time spent at 2.00-5.00 METs therefore suggest that nightly CPAP therapy in the present study resulted in a substantial 2 hours per day shift away from sleeping and/or activities involving sitting or standing quietly to those involving body movement with moderate but not vigorous exertion.

As was previously discussed (refer to *section 4.4.2.4 Daily AEE Profiles*), it was not possible to actigraphically determine in this study how much of the time was spent asleep as opposed to awake while sitting or standing with little activity when AEE was 0-1.99 METs. However, before the commencement of nightly CPAP therapy the OSA patients in this study spent an average of 89.6% of each 24 hour period (21.5 hours) engaged at an AEE of 0-1.99 METs. Polysomnographic studies with CPAP naive OSA patients have reported total sleep times of 5 to 6.5 hours (Hedli *et al.*, 2012; Loredó *et al.*, 1999; Loredó *et al.*, 2006; McArdle and Douglas, 2001). This suggests that the participants in the present study were awake and sitting or standing with little activity during most of the time when the AEE was at 0-1.99 METs.

Total sleep time per day does not change after the commencement of nightly CPAP therapy (Loredo *et al.*, 1999; Loredo *et al.*, 2006; McArdle and Douglas, 2001). This suggests that after commencement of CPAP, the OSA patients in the present study spent less time awake while quietly sitting or standing, and instead spent this time engaged in activities associated with an AEE of  $\geq 2$  METs. This CPAP related effect was especially evident on the daily AEE histograms at the very low level of 0-0.1 METs which occurred much less frequently after CPAP. One interpretation of this effect is that CPAP dramatically reduced the initially (Pre-CPAP) large amount of time that the OSA patients spent awake while in a quiescent or dormant state. However, as already discussed (refer to *section 4.4.2.4 Daily AEE Profiles*), it is unclear whether such low AEE levels reflect sleeping or awake and fully resting conditions.

The Actiheart system would register an increased heart rate or increased body movements as an increase in AEE irrespective of whether the individual being monitored was asleep or awake. This raises the possibility that heart rate and body movements in the sleeping OSA participants increased sufficiently during CPAP for the Actiheart system to register an increased AEE of  $\geq 2$  METs, and that this constitutes an alternative explanation for the CPAP related decrease in the amount of time spent at an AEE of 0-1.99 METs. However, heart rate falls acutely after commencement of CPAP therapy in OSA patients and does not differ from pre CPAP levels after 2 months of CPAP therapy (Logan *et al.*, 2003; Tkacova *et al.*, 1998). On the other hand, periodic limb movements can increase in OSA patients when CPAP is applied (Baran *et al.*, 2003; Fry *et al.*, 1989; Hedli *et al.*, 2012), although decreased periodic limb movements have also been reported (Baran *et al.*, 2003; Hedli *et al.*, 2012). Nevertheless, it seems implausible that an increase in intermittent periods of minor body movements during sleep could raise AEE sufficiently to  $\geq 2$  METs.

#### 4.4.4 Clinical Implications for OSA

OSA patients with significant comorbidities were excluded from participating in the present study. However, OSA is a risk factor for a range of chronic disorders and adverse health outcomes, including hypertension (Akahoshi *et al.*, 2010; Nieto *et al.*, 2000; Parish and Shepard, 1990; Peppard *et al.*, 2000; Silverberg *et al.*, 2002), cardiovascular disease (Marin *et al.*, 2005), glucose intolerance, insulin resistance and type 2 diabetes (Akahoshi *et al.*, 2010; Punjabi *et al.*, 2004; West *et al.*, 2006) and death from cardiovascular events (Marin *et al.*, 2005; Parish and Shepard, 1990). The available evidence in the literature suggests that these adverse health outcomes show significant improvements after commencement of nightly CPAP therapy (Doherty *et al.*, 2005; Harsch *et al.*, 2003; Marin *et al.*, 2005; Parish and Shepard, 1990; Silverberg *et al.*, 2002). However, the mechanism/s responsible for these improvements remains unclear (Akahoshi *et al.*, 2010; Mohan and Kumar, 2013).

Increased physical activity is associated with a range of improved health outcomes, including in hypertension (Urata *et al.*, 1987), cardiovascular disease (Hu *et al.*, 2004; Lee *et al.*, 2001; Manson *et al.*, 2002; Sesso *et al.*, 2000; Smith *et al.*, 2000; Tanasescu *et al.*, 2002), diabetes mellitus (Lynch *et al.*, 1996) and mortality (Hu *et al.*, 2004; Lee and Skerrett, 2001; Paffenbarger *et al.*, 1993; Smith *et al.*, 2000; Warburton *et al.*, 2006). As has already been discussed, these adverse health outcomes commonly afflict OSA patients. This raises the question as to whether the CPAP related increase in daily AEE in the present study was sufficient to induce improved health outcomes.

In their narrative review of the health benefits of physical activity, Warburton *et al* (2006) argued that an increase in energy expenditure of  $4,200 \text{ kJ}\cdot\text{week}^{-1}$  is associated with a 20-30% decrease in mortality from all causes. However, these authors also noted that the intensity of the physical activities responsible for the increase in energy expenditure played an important role in reducing mortality. Based on a review of the literature, the American College of Sports Medicine's 2011 position stand on the quantity and quality of exercise for maintaining health concluded that an increase in weekly energy expenditure of  $4,200 \text{ kJ}\cdot\text{week}^{-1}$  is associated with reduced rates of cardiovascular disease and premature mortality if the physical activities are sufficiently intense to raise the total energy expenditure to 3-5.9 METs. This position stand article further argued that reduced risks occur with increases in BEE of as low as  $2,100 \text{ kJ}\cdot\text{week}^{-1}$ . In view of these considerations, the CPAP related increase in AEE of  $3,501 \text{ kJ}\cdot\text{day}^{-1}$  ( $24,507 \text{ kJ}\cdot\text{week}^{-1}$ ) at AEE levels of 1.4 to 3.2 METs (total BEE of 2.4 to 4.2 METs) in the present study may have been sufficient to significantly improve health outcomes in a range of chronic conditions that are associated with OSA. It is of interest to speculate that, such improvements could potentially contribute to the improved health outcomes in comorbidities in OSA patients that have been broadly attributed to CPAP in other studies.

Increased BMI and obesity are associated with a range of chronic disorders and adverse health outcomes, including hypertension, cardiovascular disease and type 2 diabetes (Ali and Crowther, 2005; Hu *et al.*, 2004; Kopelman, 2007; Wellman and Friedberg, 2002). Obesity is also an important risk factor for OSA and many OSA patients are overweight (Ali and Crowther, 2005; Young *et al.*, 2005; Young *et al.*, 1993). Indeed, using criteria from the World Health Organization (World Health Organization, 2000), 1 of the 8 participants (12.5%) in the present study was overweight (BMI 25 to  $30 \text{ kg}\cdot\text{m}^{-2}$ ), 5 participants (62.5%) were moderately obese (BMI 30 to  $35 \text{ kg}\cdot\text{m}^{-2}$ ), 1 participant (12.5%) was severely obese (BMI 35 to  $40 \text{ kg}\cdot\text{m}^{-2}$ ) and 1



participant (12.5%) was very severely obese ( $\text{BMI} > 40 \text{ kg.m}^{-2}$ ) at the commencement of the present study. Increased physical activity can result in modest weight losses (U.S. Department of Health, 2008). Therefore, it could be argued that increased physical activities in OSA patients after the commencement of CPAP therapy could potentially lead to some weight loss and that this could result in improved health outcomes. However, body weight did not decrease after the commencement of CPAP therapy in the present study, and this is consistent with the findings of other studies, including studies which examined the effects of CPAP over periods of a year or longer (Drager *et al.*, 2014; Engleman *et al.*, 1996; Harsch *et al.*, 2003; Redenius *et al.*, 2008). Indeed, some studies have reported increased body weight and BMI after commencement of CPAP therapy (Drager *et al.*, 2014; Redenius *et al.*, 2008).

The time lag between reduced daytime sleepiness and increased daily AEE evident in this study suggests that reduced daytime sleepiness does not automatically and immediately translate into increased daily AEE. This raises the possibility of whether there may be a role for behavioural modification programs centered on improving daily activities to facilitate and augment the transition from reduced daytime sleepiness to increased daily AEE in OSA patients after they commence CPAP therapy. The daily AEE profile data from this study may be useful in clarifying which types of activities such behavioural modification programs should focus on. Visual comparison of the daily AEE histograms revealed that the CPAP related increase in AEE was restricted to the 1.4 to 3.2 METs range and that this effect was already evident at CPAP-1. Therefore, the findings of the present study suggest that behavioural modification programs aimed at improving daily activities should, at least initially, concentrate on encouraging modest activities in the 1.4 to 3.2 METs range, and that such programs could potentially begin to provide benefits even after only several weeks of CPAP therapy.

Actigraphy is increasingly being used in different clinical settings (Ahmed *et al.*, 2007; Beck *et al.*, 2004; Dursun *et al.*, 1999; Sadeh and Acebo, 2002). The findings of the present study have clearly demonstrated that prolonged continuous recording of Actiheart based estimates of AEE provides novel and unique insights into how CPAP therapy affects OSA patients. Moreover, the findings of the present study suggest that the Actiheart system's ability to provide continuous and prolonged moment-by-moment recordings of AEE estimates, and the ability to download such data for computerised analyses such as daily AEE profiles, makes the Actiheart system potentially useful for assessing daily activities and physical disability in a broad range of clinical settings.

#### 4.4.5 Conclusion

This is the first study to examine the effects of nightly CPAP therapy on functional activities in OSA patients using both objective and subjective validated measurements of daily activity. The Actiheart's ability to accurately and continuously estimate and digitally record AEE on a minute-by-minute basis over prolonged periods of time (days or weeks), and the ability to download such data for computerised analyses, has also for the first time enabled quantitative analysis of minute-to-minute estimates of AEE over entire 24 hour periods both before and after OSA patients commenced nightly CPAP therapy.

Daily AEE increased significantly by an average of 3,501 kJ per day and the OSA participants spent significantly more time engaged in daily activities where  $AEE \geq 2$  METs after 4-6 weeks of nightly CPAP therapy. The data suggests that CPAP therapy resulted in a substantial 2 hours per day shift away from sleeping and/or activities involving sitting or standing quietly to those involving body movement with moderate but not vigorous exertion. Daily AEE profiles revealed a preponderance of time spent at low levels of activity which is consistent with a sedentary lifestyle. In addition, a large numeric decrease in the amount of time spent at 0-0.1 METs was noted after commencement of nightly CPAP therapy, as was a small sustained increase in the amount of time spent at approximately 1.4 to 3.2 METs after commencement of nightly CPAP therapy. The results also demonstrate that the ESS, FOSQ-30 and 4 of its 5 domains each improved significantly after 4-6 weeks of nightly CPAP therapy, a finding that is consistent with the results of previous studies.

The findings of this study suggest that excessive daytime sleepiness plays a role in decreased functional activities in OSA patients and that CPAP therapy can increase functional activities by improving excessive daytime sleepiness. In addition, it is plausible that the increased amount of time engaged in physical activity where  $AEE \geq 2$  METs after the commencement of nightly CPAP therapy may improve adverse health outcomes which relate to comorbidities that commonly afflict OSA patients. The contribution that such improvements could potentially make to the improved health outcomes that have been attributed to CPAP in other studies is not known and warrants further study.

Statistically significant improvements were not evident in the daily AEE or the time engaged in daily activities where  $AEE \geq 2$  METs after only 1-2 weeks of nightly CPAP therapy. Improvements in these variables lagged behind that for the ESS, the FOSQ-30 and its domains. The delayed improvements in daily AEE and the amount of time spent at daily activities where  $AEE \geq 2$  METs may theoretically reflect a slower onset of behavioural changes in daily activities when excessive daytime sleepiness is reduced. This possibility serves to illustrate the potential benefits of including actigraphic estimates of daily AEE to provide more comprehensive monitoring of functional outcomes in OSA patients receiving CPAP therapy.

The time lag between reduced daytime sleepiness and increased daily AEE evident in this study suggests that reduced daytime sleepiness does not automatically and immediately translate into increased daily AEE. This raises the possibility of whether there may be a role for behavioural modification programs centered on improving daily activities to facilitate and augment the transition from reduced daytime sleepiness to increased daily AEE in OSA patients after they commence CPAP therapy. The daily AEE profile data from this study may be useful in clarifying which types of activities such behavioural modification programs should focus on.

Visual comparison of the daily AEE histograms revealed that the CPAP related increase in AEE was restricted to the 1.4 to 3.2 METs range and that this effect was already evident at CPAP-1. Indeed, as the CPAP related increase in AEE was restricted to the 1.4 to 3.2 METs range and this effect was already evident at CPAP-1, it can be argued that behavioural modification programs aimed at improving daily activities should, at least initially, concentrate on encouraging modest activities in the 1.4 to 3.2 METs range, and that such programs could potentially begin to provide benefits even after only several weeks of CPAP therapy.

Overall, the results of this study clearly demonstrated that prolonged continuous recording of Actiheart based estimates of AEE can provide more comprehensive monitoring of functional outcomes in OSA patients receiving CPAP therapy, as well as providing novel and unique insights into how CPAP therapy affects OSA patients. From a broader clinical perspective, the findings of the present study suggest that the Actiheart system's ability to provide continuous and prolonged minute-by-minute recordings of AEE estimates, and the ability to download such data for computerised analyses such as daily AEE profiles, makes the Actiheart system a potentially useful tool for assessing daily activities and physical disability in a broad range of clinical settings.

## Chapter 5 General Discussion

The studies in this thesis were prompted by novel opportunities that have arisen as a result of the rapidly emerging field of actigraphy which allows noninvasive and nonintrusive assessment of physical activity. These advances have enabled exercise and health professionals to continuously monitor body movements and BEE over prolonged periods in unrestricted free-living conditions. These features provide a unique opportunity to use actigraphic techniques for research and clinical purposes, especially with patients who have diseases that impair their daily physical activities.

In recent years, technological improvement have led to the monitoring of heart rate and/or body movement with accelerometers using small portable devices which provide accurate long-term objective assessment of physical activity. Several accelerometric devices are currently commercially available for indirectly estimating body energy expenditure. Of these devices, the Actiheart appears to be the most accurate over a wide range of different types of physical activities. The superior accuracy stems from the fact that the Actiheart system utilises measurements of both heart rate and body movement with separate dimensional accelerometers. Although a small number of studies have already demonstrated that the Actiheart provides accurate estimates of body energy expenditure, the Actiheart system is a relatively new device and several versions have been released commercially (Crouter *et al.*, 2008). It was therefore considered prudent to first evaluate the accuracy of newly acquired Actiheart systems in our laboratory against a gold standard measurement of BEE (i.e. indirect calorimetry with oxygen consumption) before commencing studies focusing on patients who have diseases that impair their daily physical activities.

## 5.1 Accuracy of Actiheart Derived Estimates of Body Energy Expenditure During Rest and Treadmill Exercise

In light of the above mentioned considerations, a pilot study (Study 1 described in Chapter 2) was carried out to determine the accuracy of the Actiheart derived BEE estimates using a group based equation during rest and treadmill exercise in healthy participants. The pilot study also examined whether the chest straps from the mobile telemetric Oxycon mobile system used to measure oxygen consumption interfered with the function of the Actiheart's accelerometers, and whether the telemetric Oxycon signals produced electrical interference on the Actiheart's heart rate electrodes. For this purpose, six healthy men each underwent the following rest and exercise protocol while data was simultaneously recorded by both the Actiheart and Oxycon Mobile systems: 1) three minutes of rest while sitting, 2) three minutes of rest standing quietly on a treadmill, 3) three minutes of treadmill walking at 3 km.hr<sup>-1</sup>, 4) three minutes of treadmill walking at 5 km.hr<sup>-1</sup> and 5) three minutes of treadmill walking at 7 km.hr<sup>-1</sup> with the treadmill at zero inclination. These resting and low to modest levels of exercise intensity were chosen because they were likely to be relevant to the normal daily behavior of patients with impaired physical capacity.

The results of this study revealed a high level of accuracy in the Actiheart derived estimates of BEE when these were compared with simultaneous measurements of BEE obtained by indirect calorimetry under conditions of rest and low to modest intensities of treadmill walking. The present study also confirmed the report by a previous published study that the Actiheart continues to provide accurate BEE estimates when a group based equation was used instead of the time consuming process of individually calibrating each experimental participant with graded exercise workloads. No evidence of mechanical or electrical interference in the Actiheart signal from the Oxycon Mobile system was found in this study. The high level of accuracy in the Actiheart derived estimates of BEE in this study supports the findings of previous

published studies. However, the current preliminary study only investigated treadmill walking and further research needs to be carried out to determine how the accuracy of Actiheart BEE estimates is influenced by different types of exercise.

## **5.2 Accuracy of Actiheart Derived Estimates of Body Energy Expenditure During Different Types of Exercise**

Studies that have examined Actiheart accuracy have mostly focused on walking. Walking was also the only type of physical activity examined in the first study in this thesis. In addition, the physical activities used in these studies were not carried out under rigidly standardised conditions such as can only be done when the precise mechanical workload is known (e.g. bicycle or arm ergometry). Exercise involving different large muscle groups can also elicit different HR and accelerometer responses, and these could potentially influence the accuracy of Actiheart based BEE estimates. It was therefore considered prudent to conduct a study to investigate Actiheart accuracy during a range of physical activities involving different muscle groups under matched mechanical workloads.

The second study in this thesis (described in Chapter 3) examined the accuracy of the Actiheart based estimates of BEE during low and moderate intensity physical activities that utilised different muscle groups (bicycle and arm ergometry) at known mechanical workloads and during matched levels of treadmill walking. Particular attention was also given to whether the higher heart rate responses during arm based exercise reported in other studies adversely impacted on the accuracy of Actiheart based estimates of body energy expenditure.

For the purposes of this study, ten healthy men each underwent the following rest and exercise protocol while data was simultaneously recorded by both the Actiheart and Oxycon



Mobile systems: 1) three minutes under resting conditions, 2) three minutes of arm or bicycle ergometry exercise at  $150 \text{ kpm}\cdot\text{min}^{-1}$  or a matched treadmill walking speed of  $3 \text{ km}\cdot\text{min}^{-1}$ , 3) three minutes of arm or bicycle ergometry exercise at  $300 \text{ kpm}\cdot\text{min}^{-1}$  or a matched treadmill walking speed of  $5 \text{ km}\cdot\text{hr}^{-1}$ , and 4) three minutes of arm or bicycle ergometry exercise at  $600 \text{ kpm}\cdot\text{min}^{-1}$  or a matched treadmill walking speed of  $7 \text{ km}\cdot\text{hr}^{-1}$  (all treadmill walking carried out at zero incline).

The results of this study revealed that the Actiheart provided accurate estimates of BEE under resting conditions and during each workload for each of the 3 types of exercise examined in this study. This finding supports the results of a growing number of studies that have examined the accuracy of Actiheart based estimates of BEE over a wide range of free living activities. Matching of indirect calorimetric based measurements of BEE between the 3 types of exercise at equivalent workloads was slightly reduced at the highest workload, but even then the Actiheart continued to provide estimates of BEE which agreed very closely with the simultaneous indirect calorimetric based measurements.

### **5.3 The Effects of CPAP on Sleepiness and Daily Activity in OSA**

Actigraphy is increasingly used in a diverse range of clinical settings. This raises the question as to which clinical condition and therapy would best be evaluated by Actiheart based estimates of BEE for the purposes of this thesis. Excessive daytime sleepiness is a cardinal feature of OSA, and it has been argued that this may play a role in decreased functional activities in OSA patients. Furthermore, excessive daytime sleepiness in OSA patients rapidly reverses after commencement of nightly CPAP therapy. It is therefore plausible that OSA patients become more active after commencement of CPAP because of reduced daytime sleepiness. Moreover, the rapid

and often marked reversal of excessive daytime sleepiness after the commencement of nightly CPAP therapy could potentially be an ideal therapeutic response for the purposes of exploring improvements in Actiheart based estimates of body energy expenditure under clinical conditions.

The possibility that OSA patients become more active after commencement of CPAP does not appear to have been rigorously investigated to date because technical limitations have until recently precluded making the necessary continuous prolonged measurements of BEE under free living conditions. Such technical limitations have also ensured that little is known concerning the profile of daily BEE in either healthy or diseased free living individuals. Importantly, these limitations have recently been overcome with the commercial release of the Actiheart system which can accurately and continuously estimate and digitally record daily energy expenditure over prolonged periods of time (days or weeks). In addition, with suitable computerised data handling procedures, the Actiheart system can also quantitatively map out how BEE varies from minute-to-minute over entire 24 hour periods.

In view of these considerations, a study (Study 3 described in Chapter 4) was carried out to examine the daily BEE and the daily BEE profile in a group of OSA patients, and to determine whether nightly CPAP therapy resulted in increased levels of daily energy expenditure and a shift in the daily BEE profile with more time spent at higher levels of physical activities. This constitutes the first study to examine the effects of nightly CPAP therapy on functional activities in OSA patients using both objective and subjective validated measurements of daily activity.

The daily AEE profiles revealed a preponderance of time spent at low levels of activity which is consistent with OSA patients adopting a sedentary lifestyle. The results of this study also demonstrate that daily AEE in each OSA patient increased significantly by an average of 3,501 kJ

per day after 4-6 weeks of nightly CPAP therapy, with significantly more time engaged in daily activities at an AEE  $\geq 2$  METs. The data suggests that CPAP therapy resulted in a substantial 2 hours per day shift away from sleeping and/or activities involving sitting or standing quietly, to those involving body movement with moderate but not vigorous exertion. In addition, a large numeric decrease in the amount of time spent at a very low AEE of 0-0.1 METs was noted after commencement of nightly CPAP therapy, as was a small sustained increase in the amount of time spent at approximately 1.4 to 3.2 METs after commencement of nightly CPAP therapy. The results also revealed CPAP related improvements in subjective self-assessment measures of sleepiness and daily functional outcomes, with significant improvements observed in the ESS, FOSQ-30 and 4 of the 5 FOSQ domains after the commencement of nightly CPAP therapy, a finding that is consistent with the results of previous studies.

The findings of this study suggest that excessive daytime sleepiness played a role in decreased daily activities in the OSA patients and that CPAP therapy increased daily activities as a result of improved excessive daytime sleepiness. In addition, it is plausible that the increased amount of time engaged in physical activity where AEE  $\geq 2$  METs after the commencement of nightly CPAP therapy may improve adverse health outcomes which relate to comorbidities that commonly afflict OSA patients. The contribution that such improvements could potentially make to the improved health outcomes that have been attributed to CPAP in other studies is not known and warrants further study. Of interest, although daily AEE increased, body weight did not decrease after 4-6 weeks of CPAP, a finding that is consistent with the results of previous studies.

Statistically significant improvements were evident in the ESS, FOSQ-30 and 4 of the 5 FOSQ domains after only 1-2 weeks of nightly CPAP therapy. In contrast, statistically significant changes in daily AEE and in the time engaged in daily activities at an AEE  $\geq 2$  METs were only

evident after 4-6 weeks of CPAP. Improvements in daily AEE and the time engaged in daily activities at an  $AEE \geq 2$  METs therefore lagged behind that for the ESS, the FOSQ-30 and its domains. Theoretically, these delayed improvements may reflect a slower onset of behavioural changes in daily activities when excessive daytime sleepiness is reduced. This possibility serves to illustrate the potential benefits of including actigraphic AEE recordings to provide more comprehensive monitoring of functional outcomes in OSA patients receiving CPAP therapy.

The time lag between reduced daytime sleepiness and increased daily AEE evident in this study suggests that reduced daytime sleepiness does not automatically and immediately translate into increased daily AEE. This raises the possibility of whether there may be a role for behavioural modification programs centered on improving daily activities to facilitate and augment the transition from reduced daytime sleepiness to increased daily AEE in OSA patients after they commence CPAP therapy. The daily AEE profile data from this study may be useful in clarifying which types of activities such behavioural modification programs should focus on. Visual comparison of the daily AEE histograms revealed that the CPAP related increase in AEE was restricted to the 1.4 to 3.2 METs range in this study, and that this effect was already evident after only 1-2 weeks of nightly CPAP therapy. This suggests that behavioural modification programs aimed at improving daily activities should, at least initially, concentrate on encouraging modest activities in the 1.4 to 3.2 METs range, and that such programs could potentially begin to provide benefits even after only several weeks of CPAP therapy.

## **5.4 Concluding Remarks**

The results of the three experimental studies in this thesis clearly demonstrated that the Actiheart system can provide a noninvasive and nonintrusive means of obtaining prolonged and

continuous recording of accurate estimates of body energy expenditure. In addition, the Actiheart system was shown to provide a more comprehensive and objective monitoring of functional outcomes in OSA patients receiving CPAP therapy, as well as providing novel and unique insights into how CPAP therapy affects OSA patients. The accurate, continuous and prolonged minute-by-minute recordings of AEE estimates, and the ability to download such data for computerised analyses such as daily AEE profiles, makes the Actiheart system a potentially useful tool for accurately and objectively assessing daily activities in a broad range of clinical settings.

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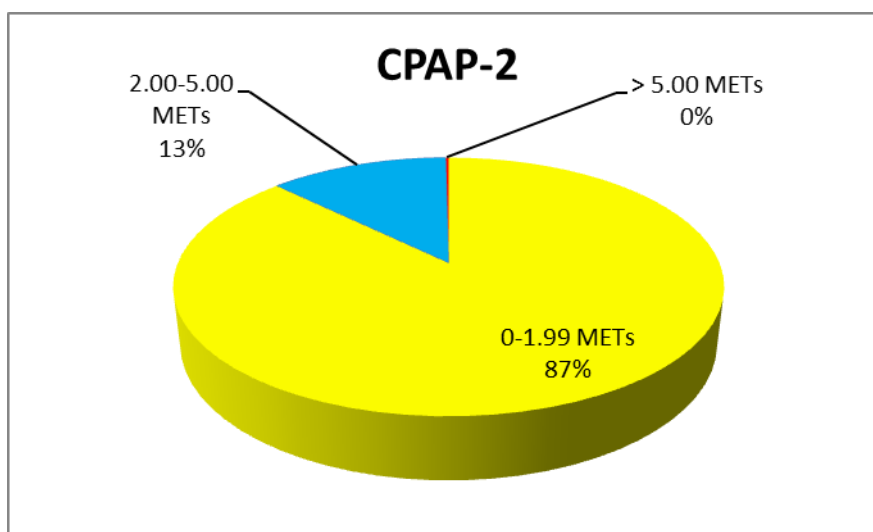
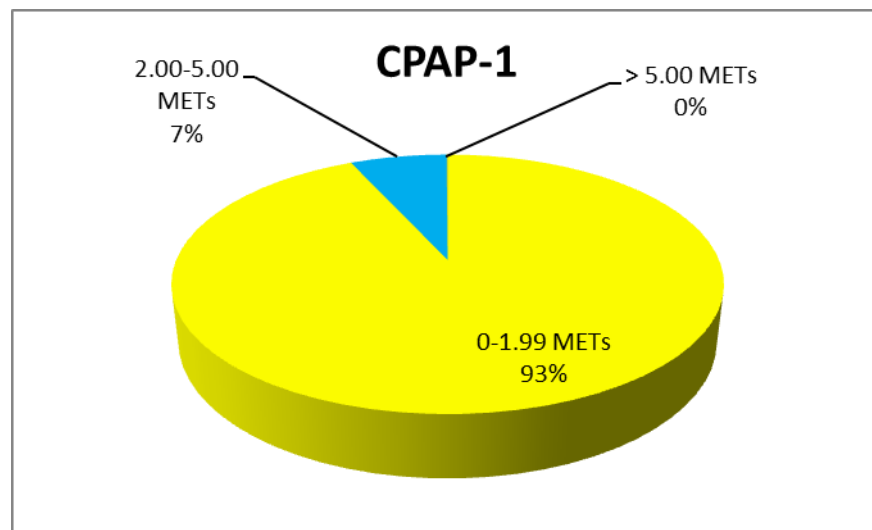
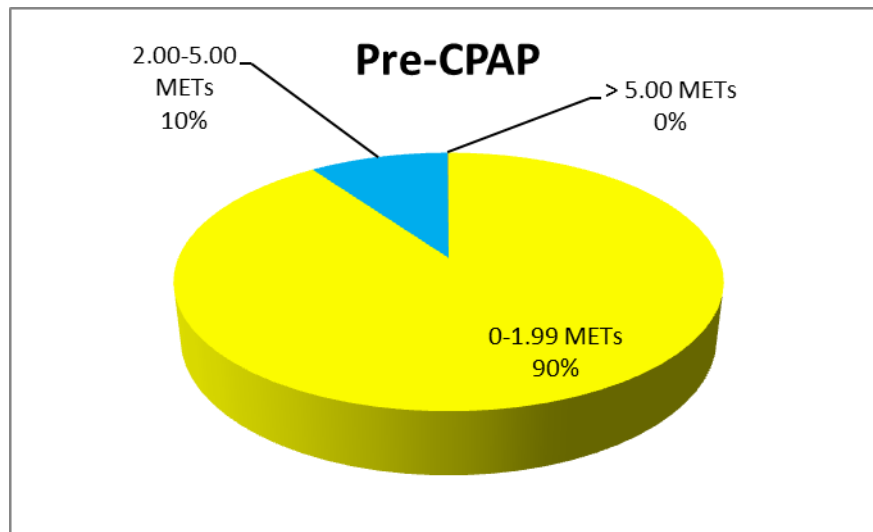
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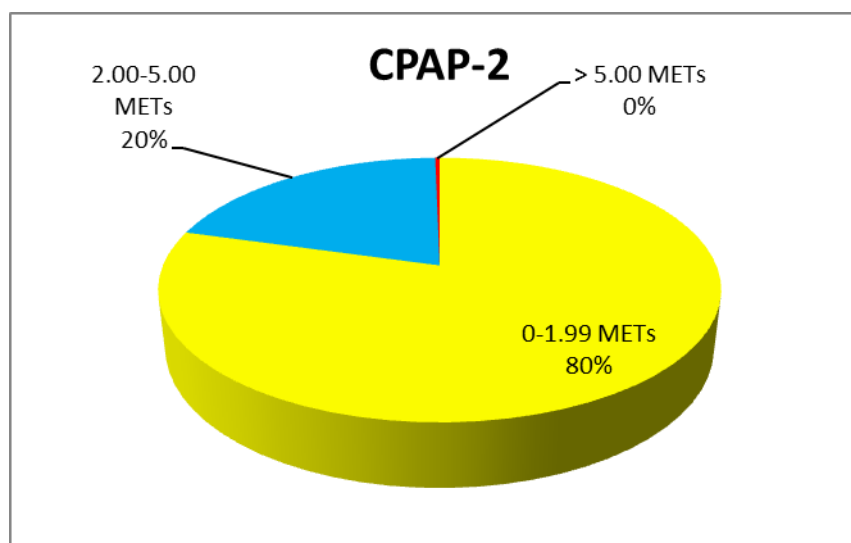
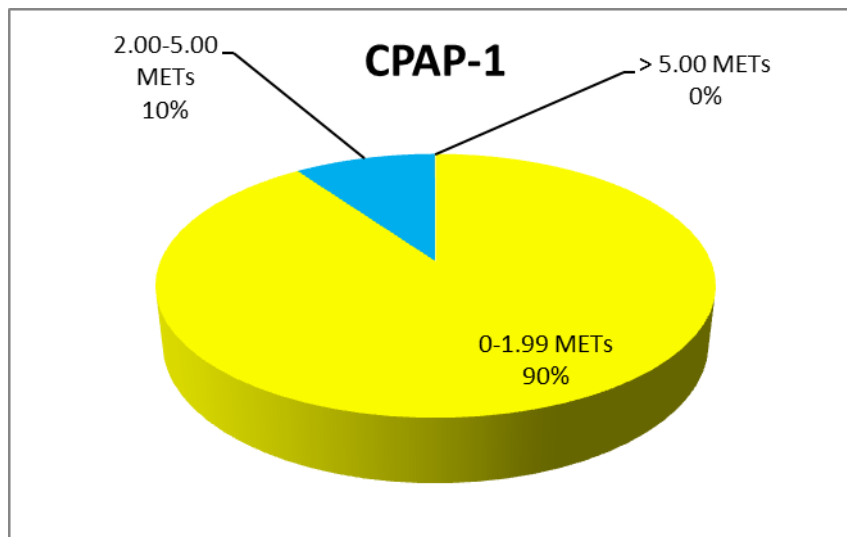
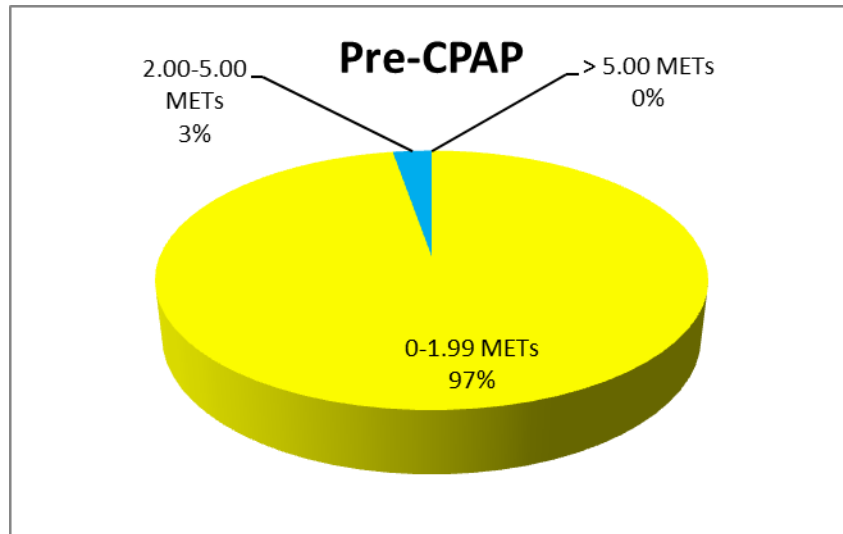
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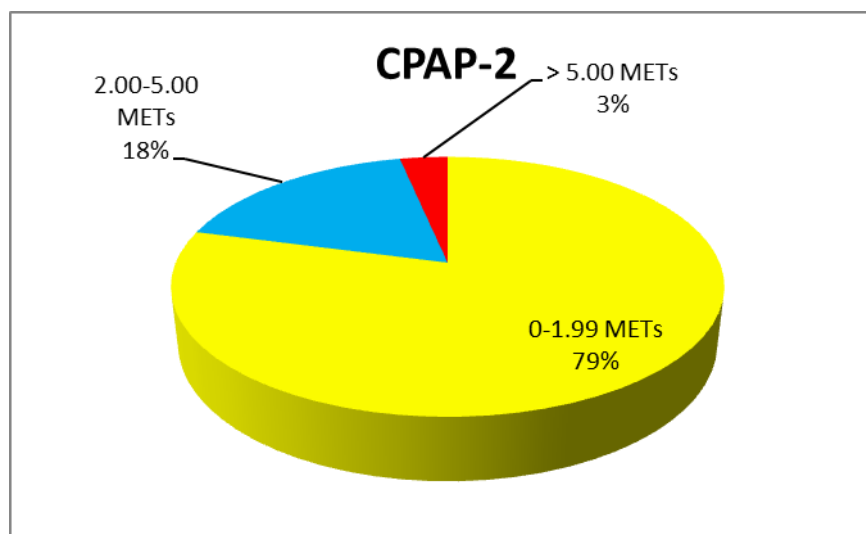
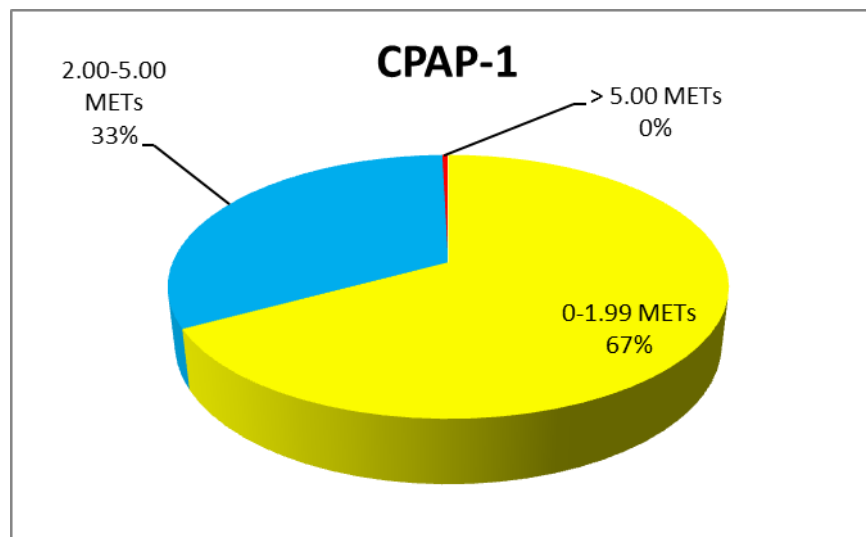
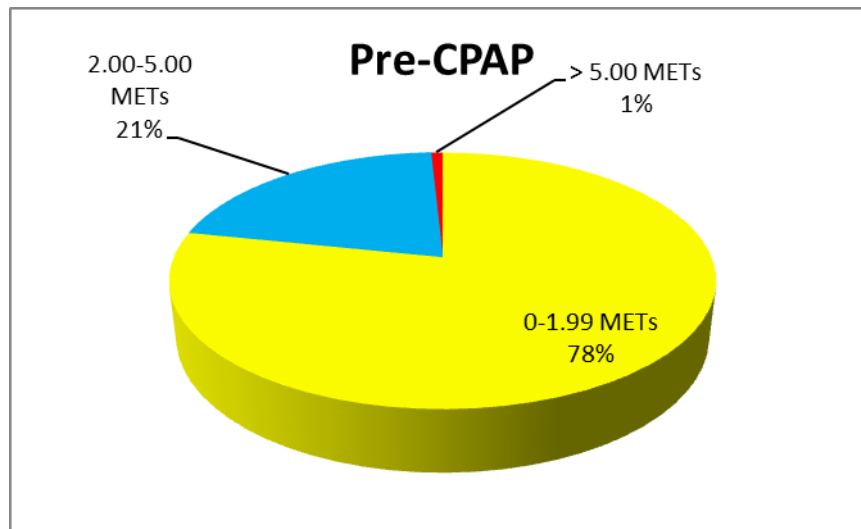
## Patient 1



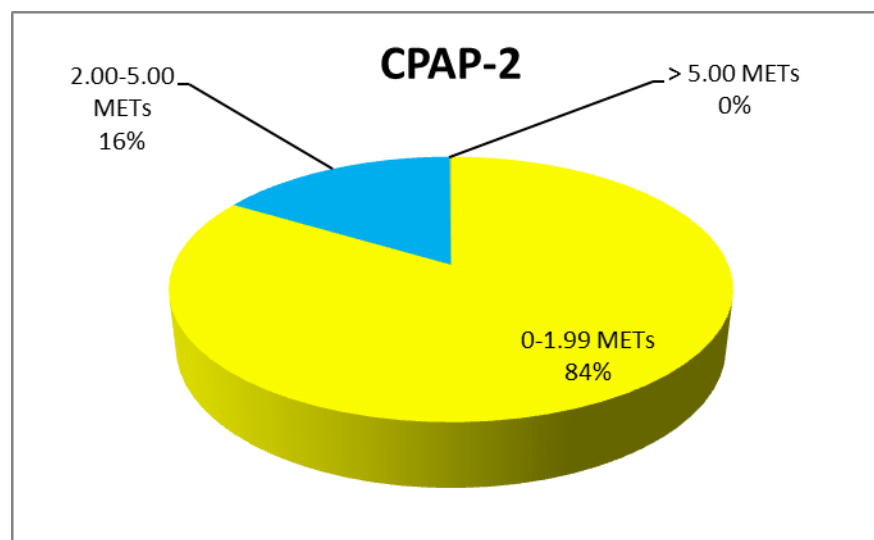
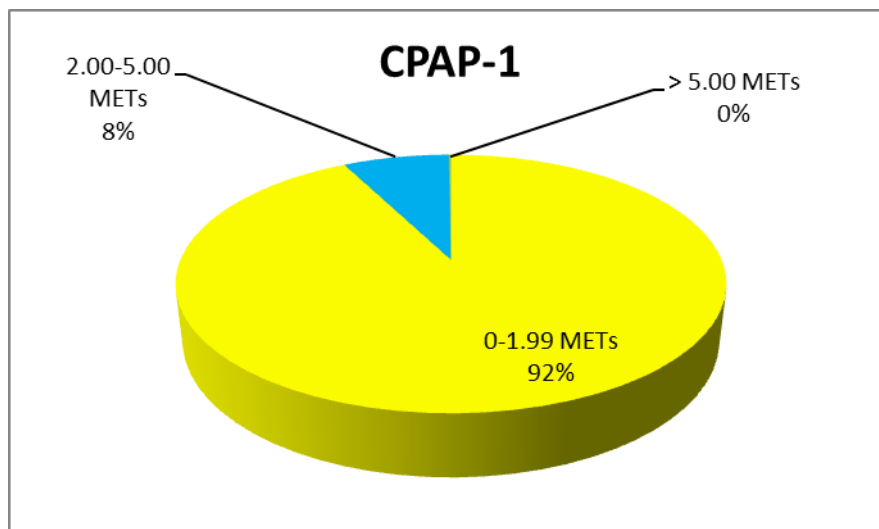
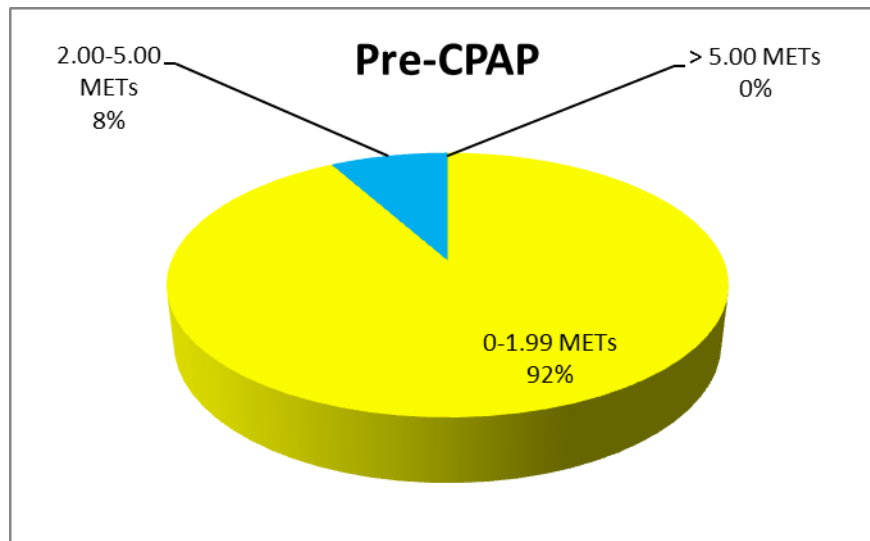
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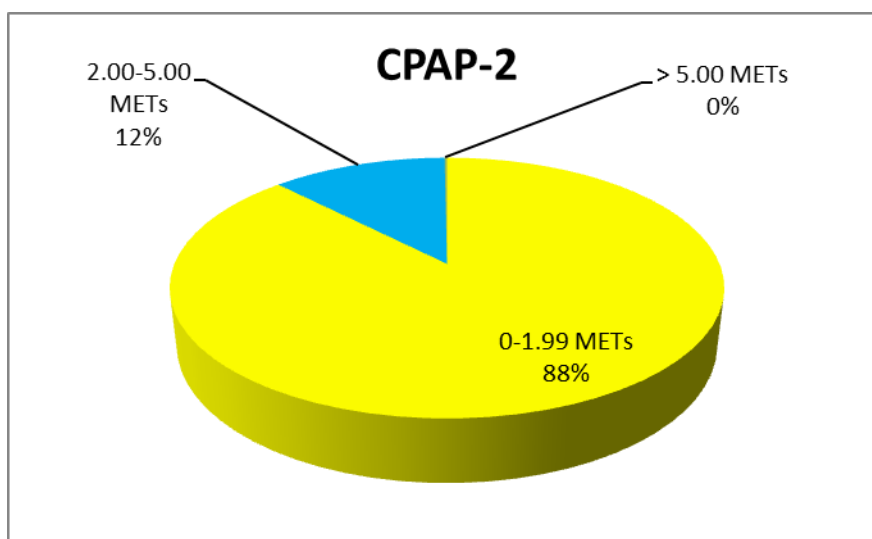
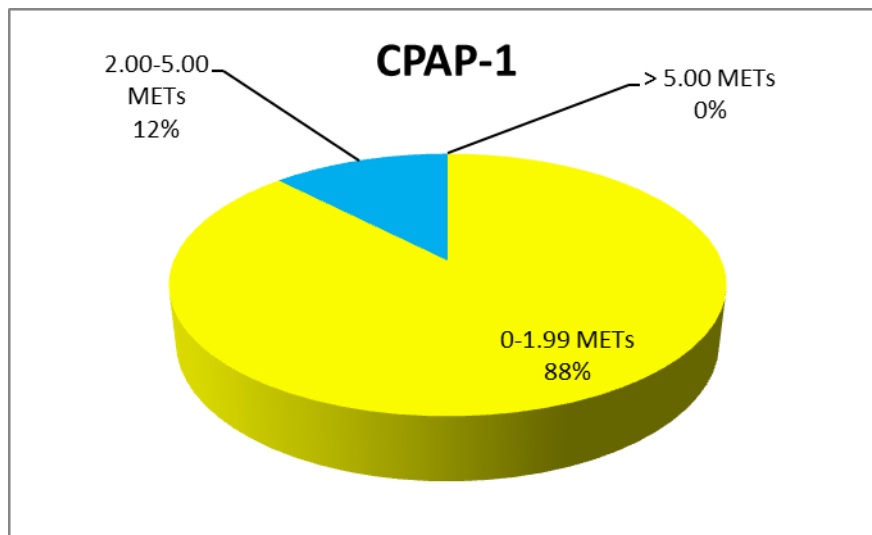
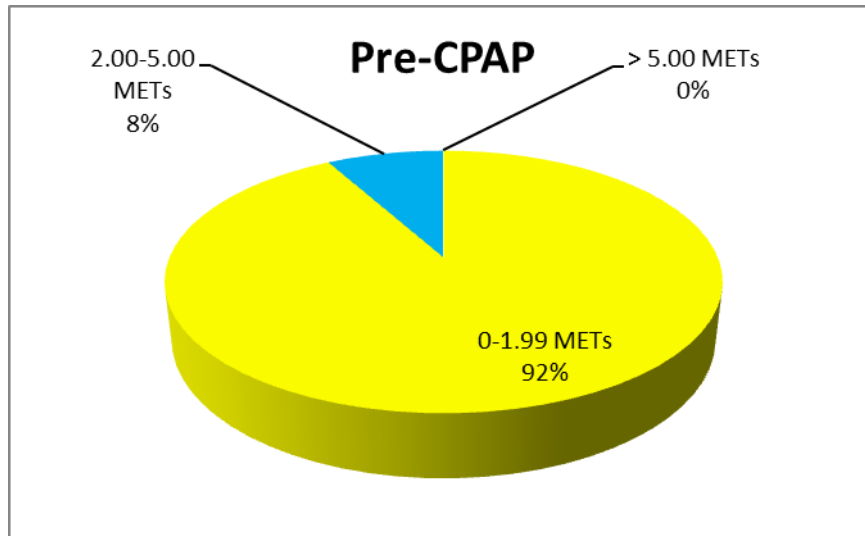
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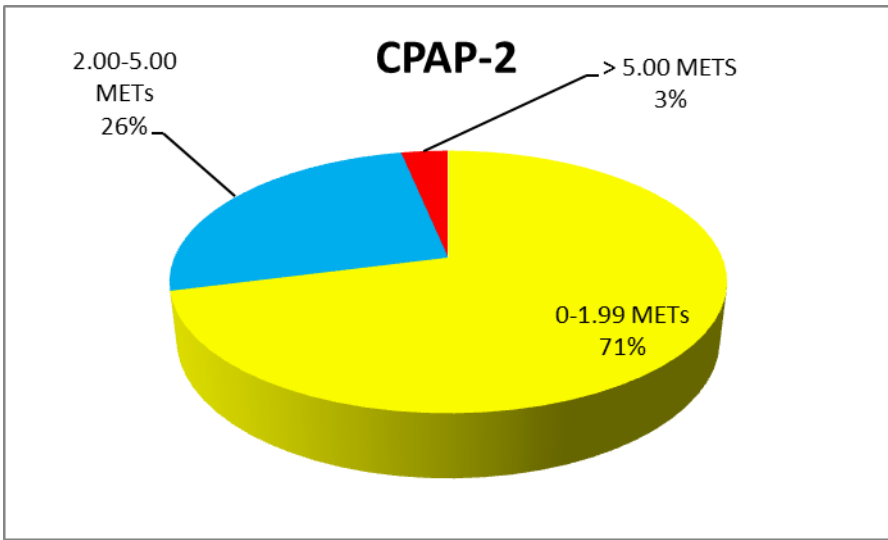
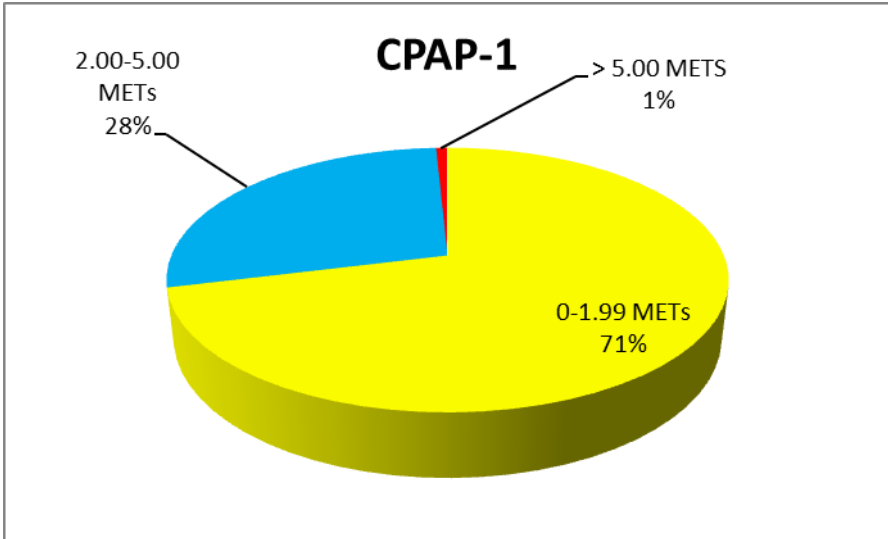
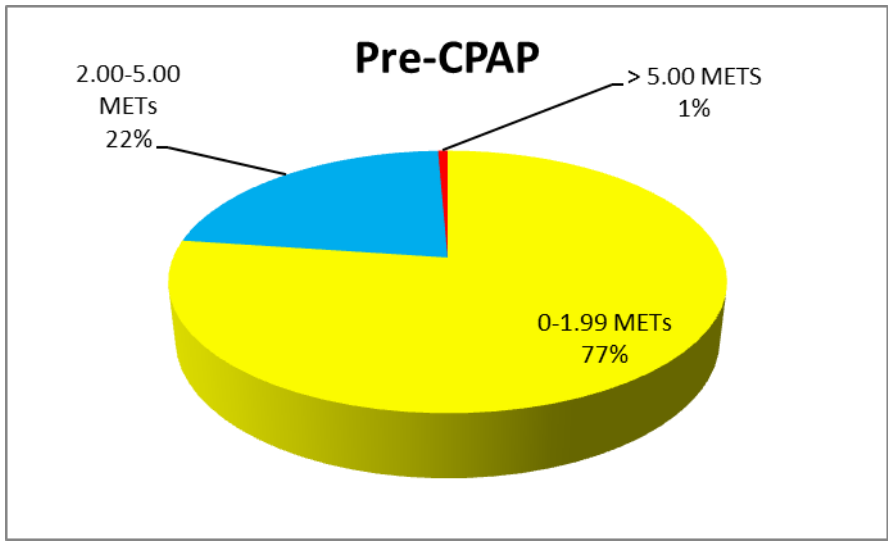
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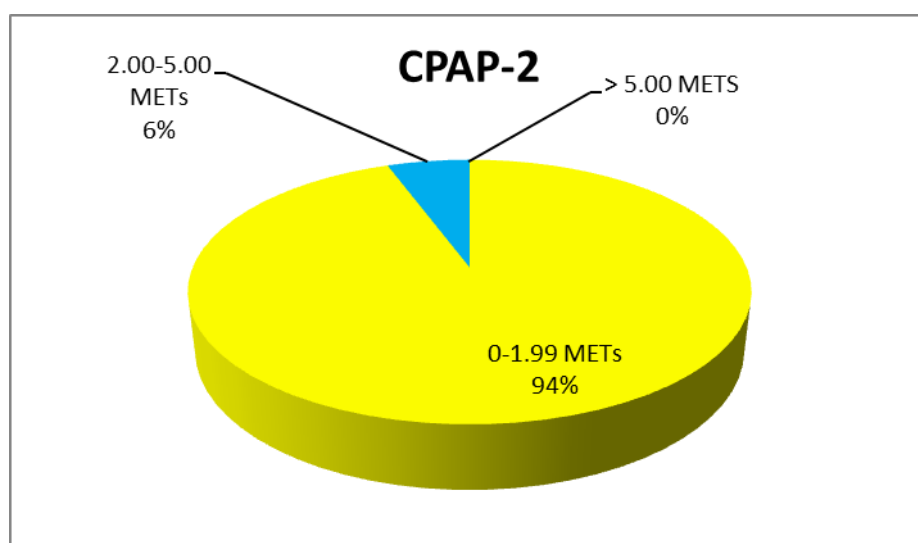
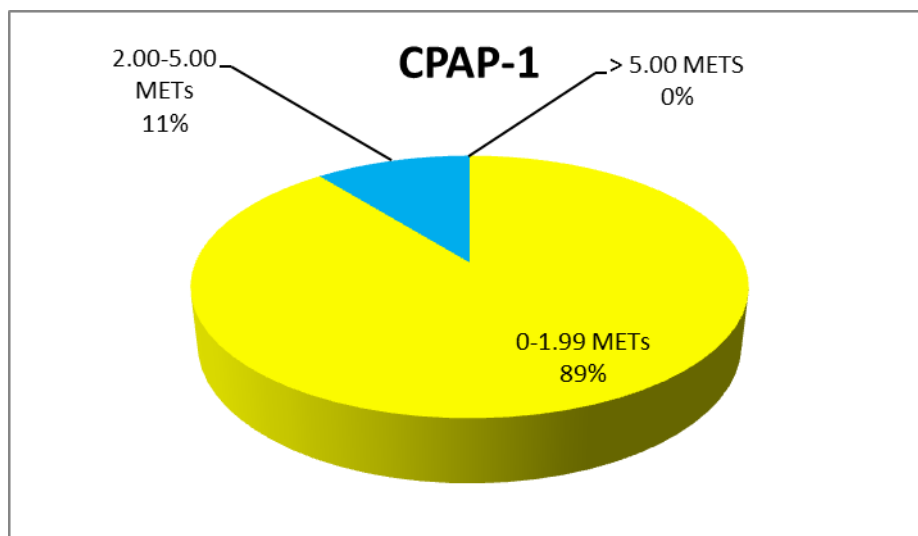
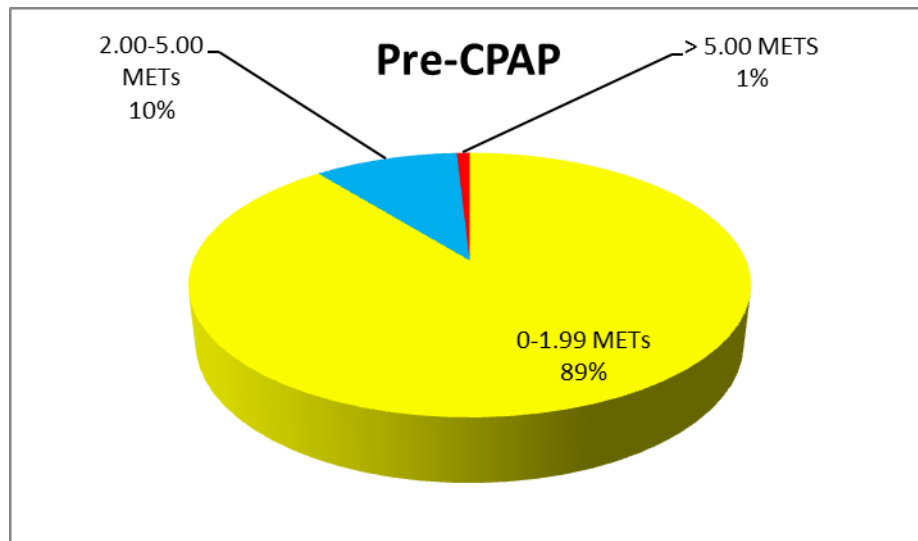
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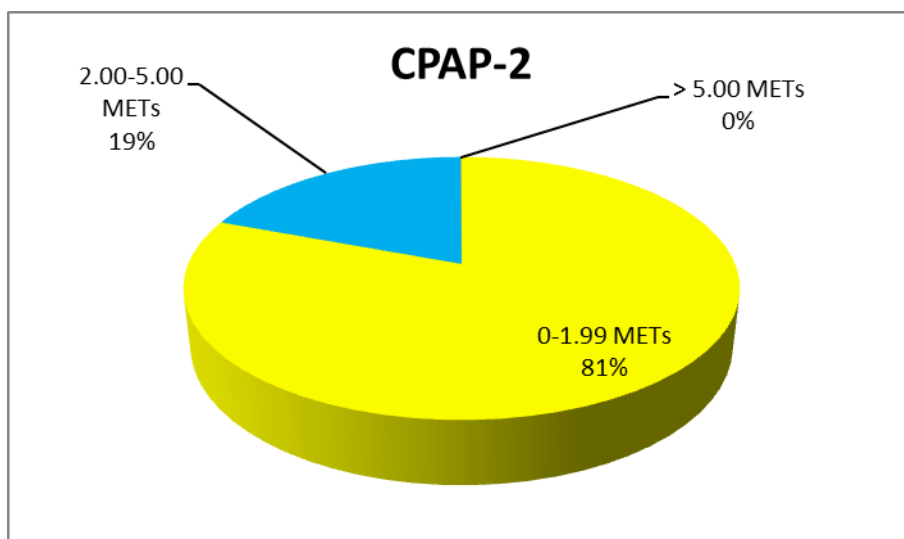
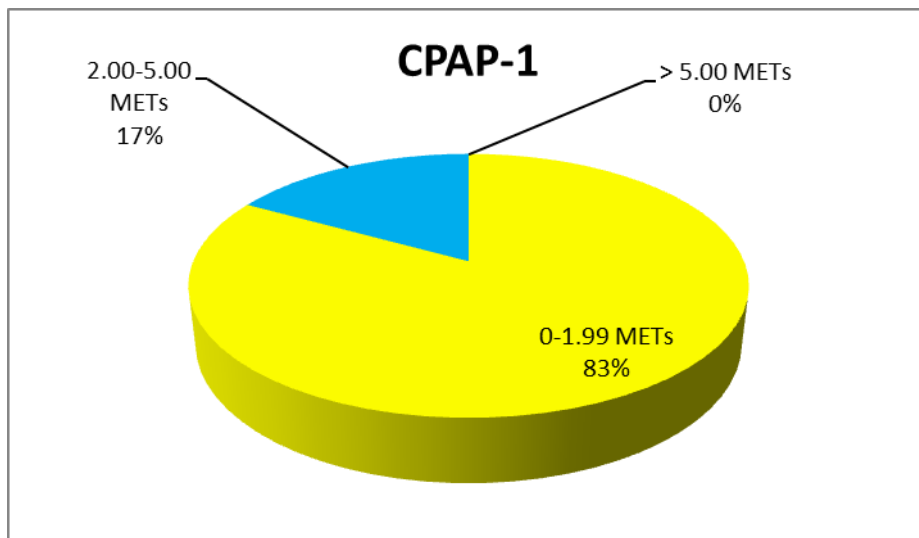
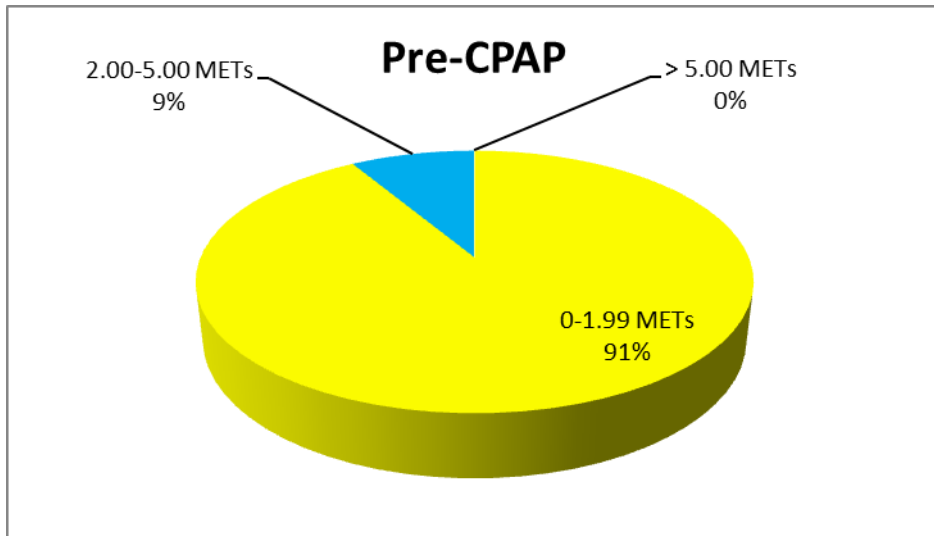
Patient 6



**Patient 7**

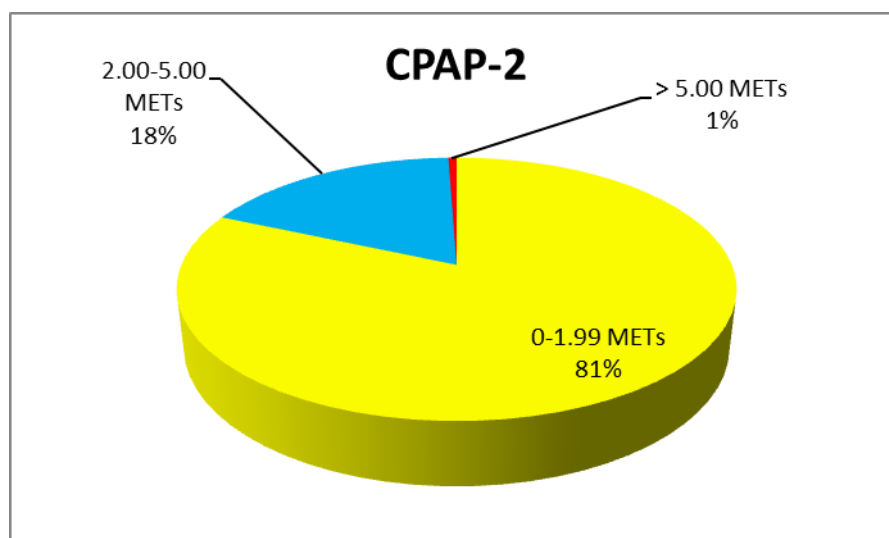
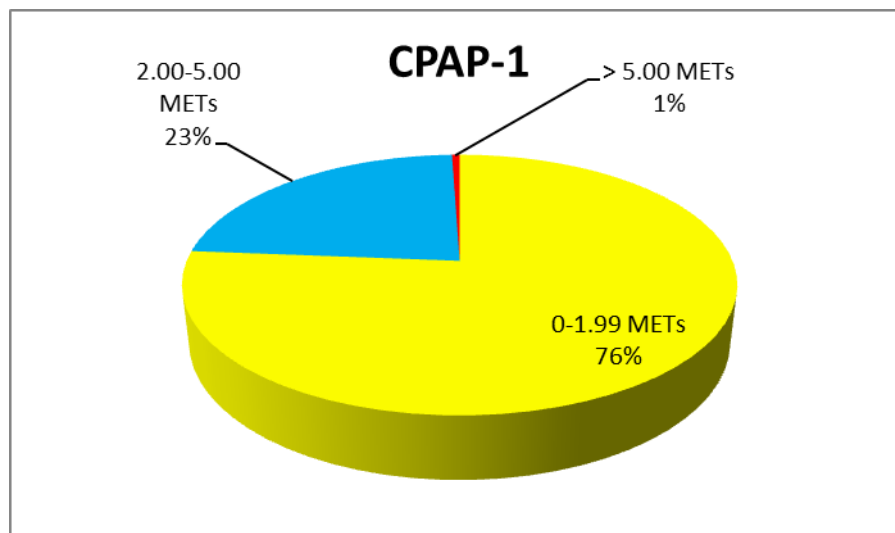
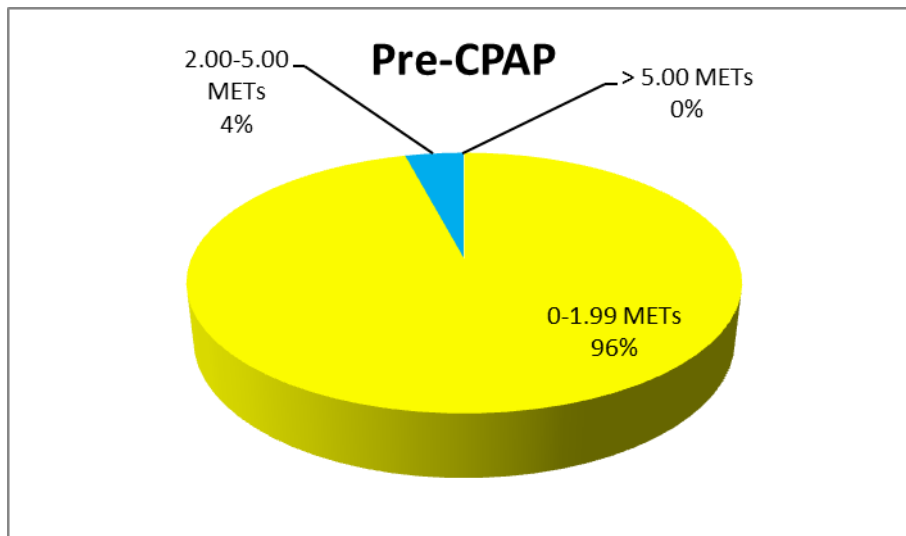


Patient 8

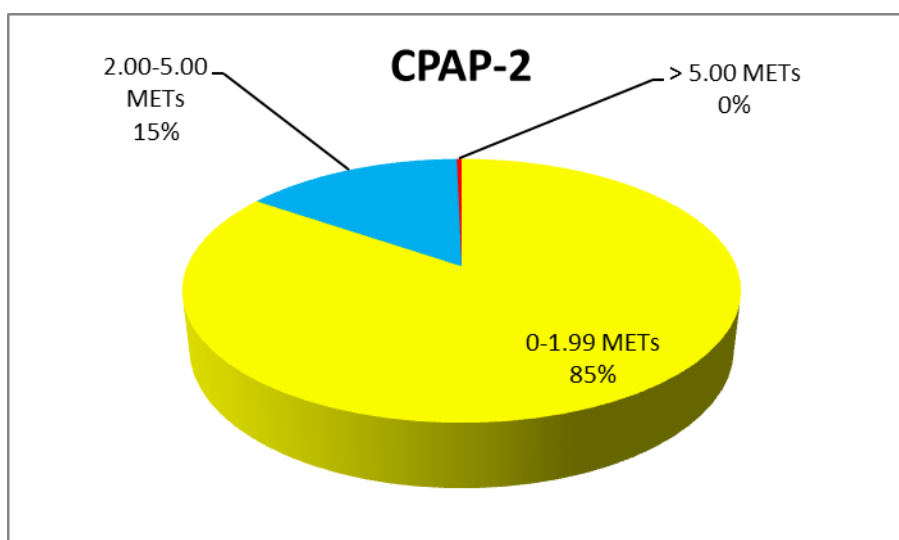
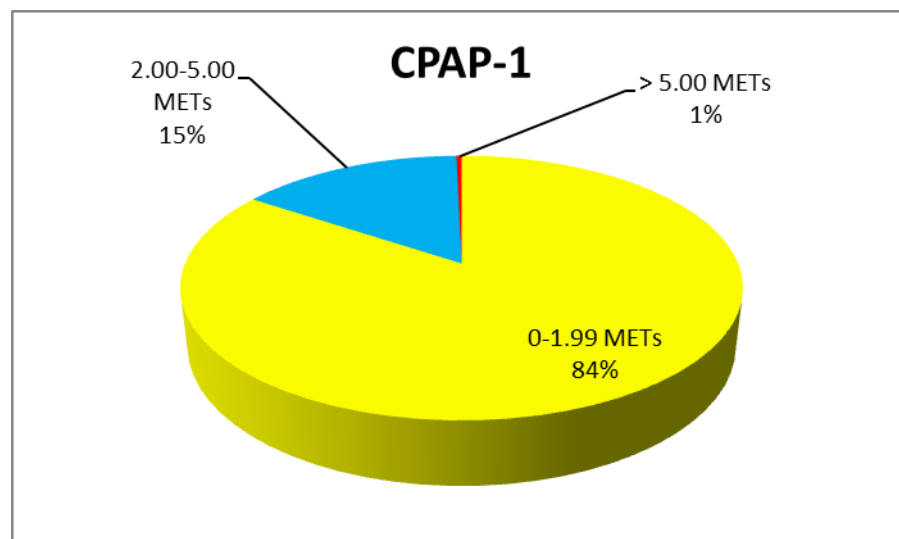
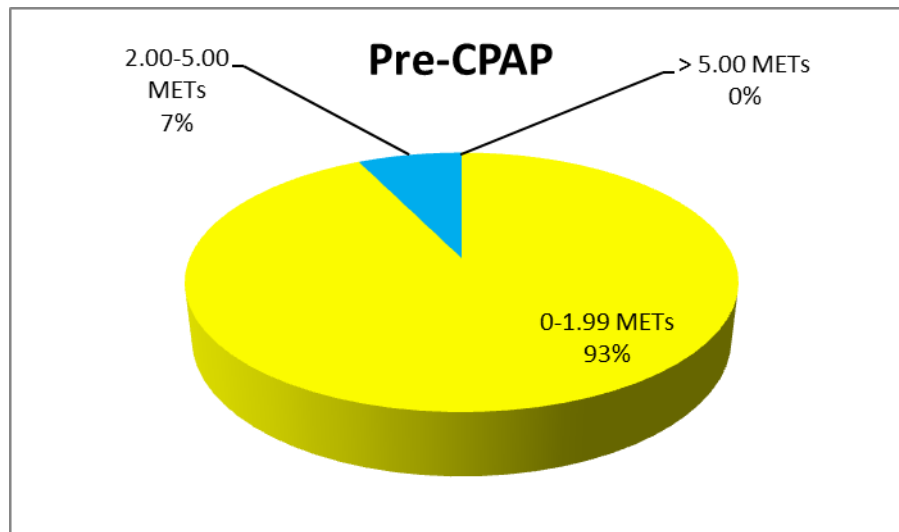




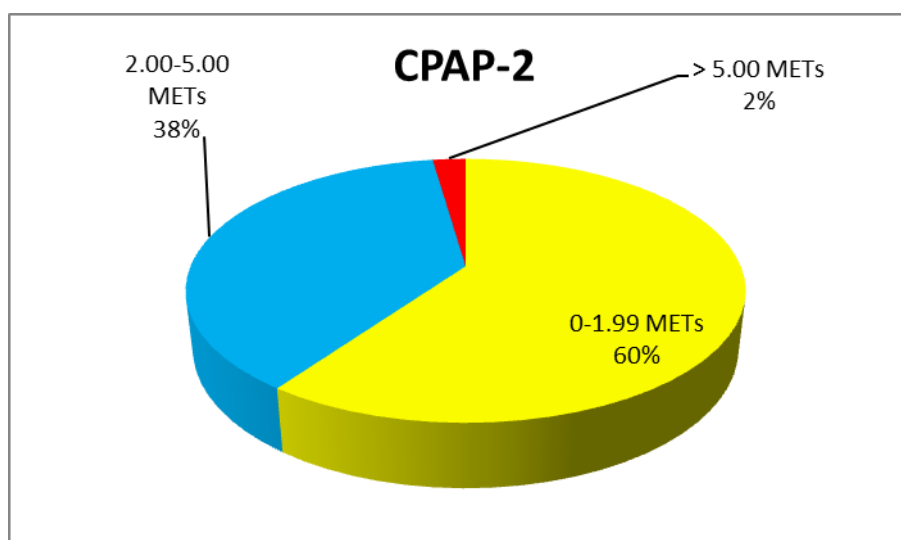
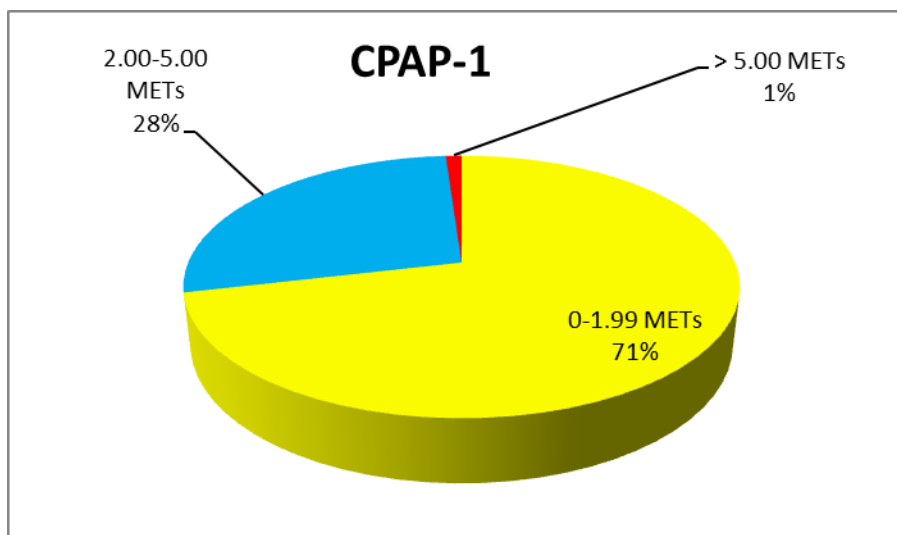
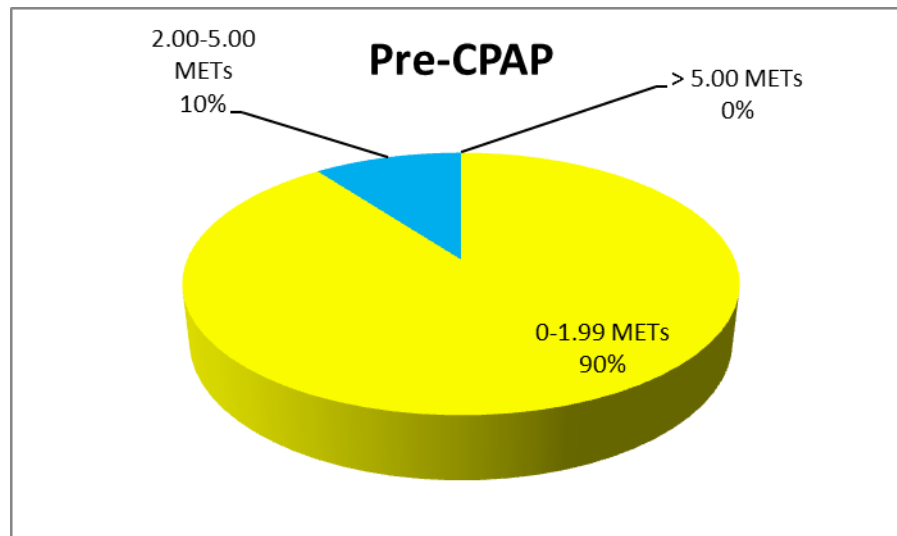
## Patient 9



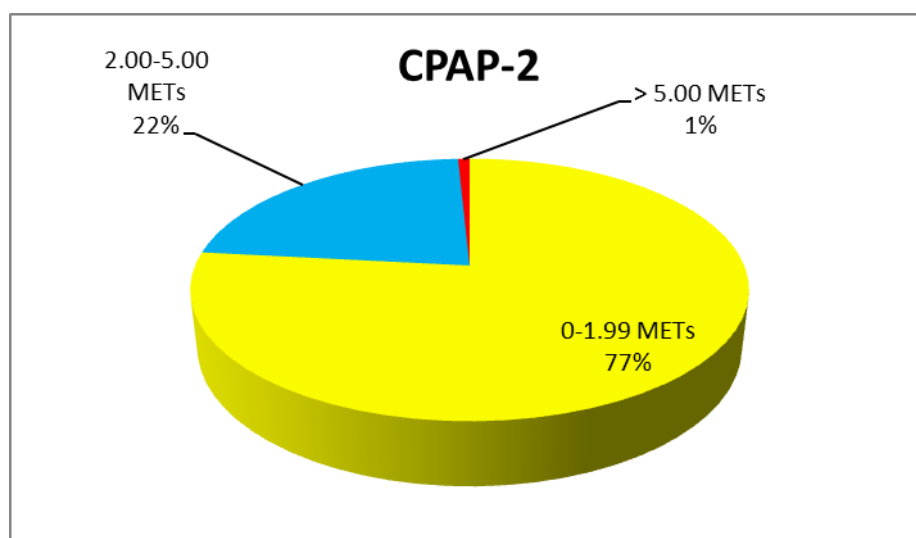
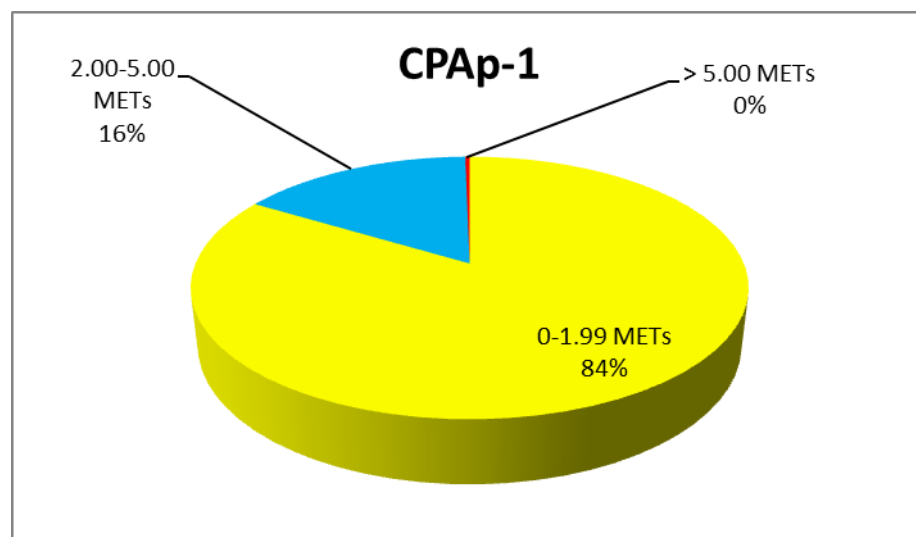
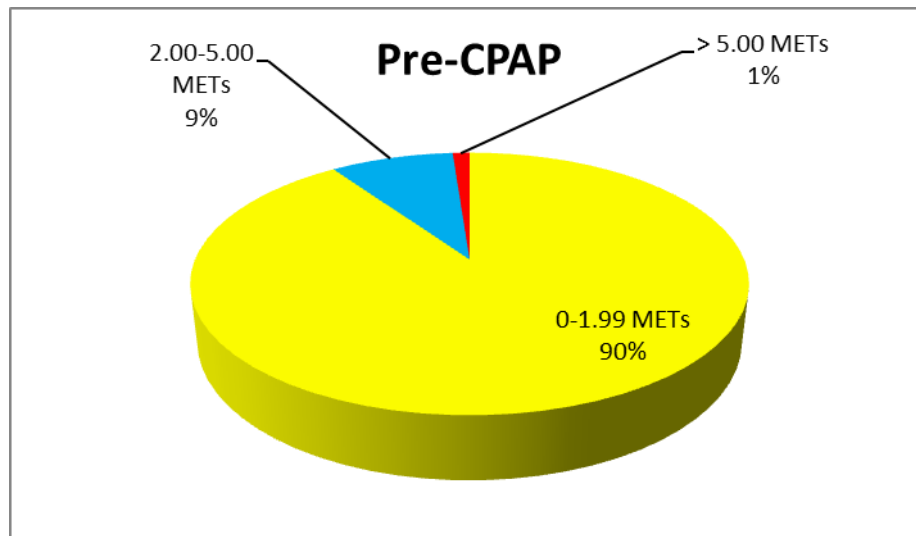
**Patient 10**



## Patient 11

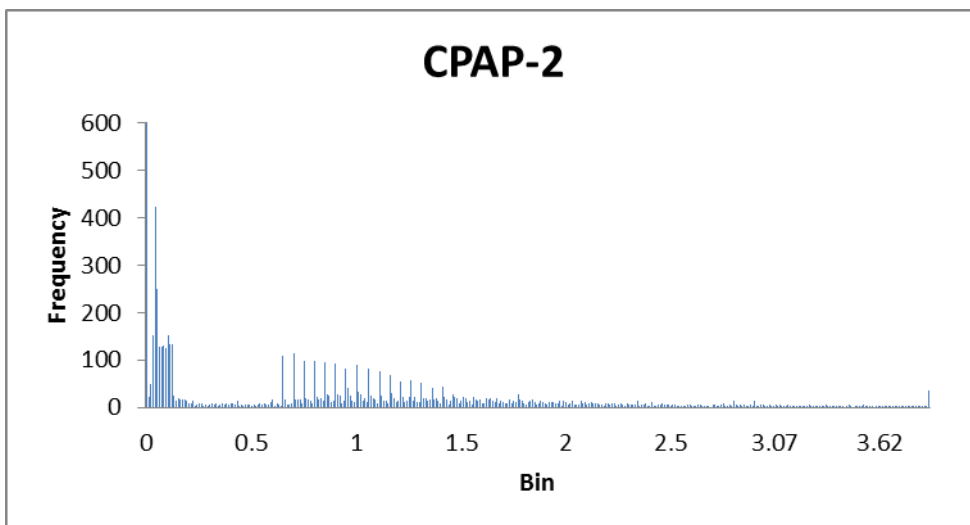
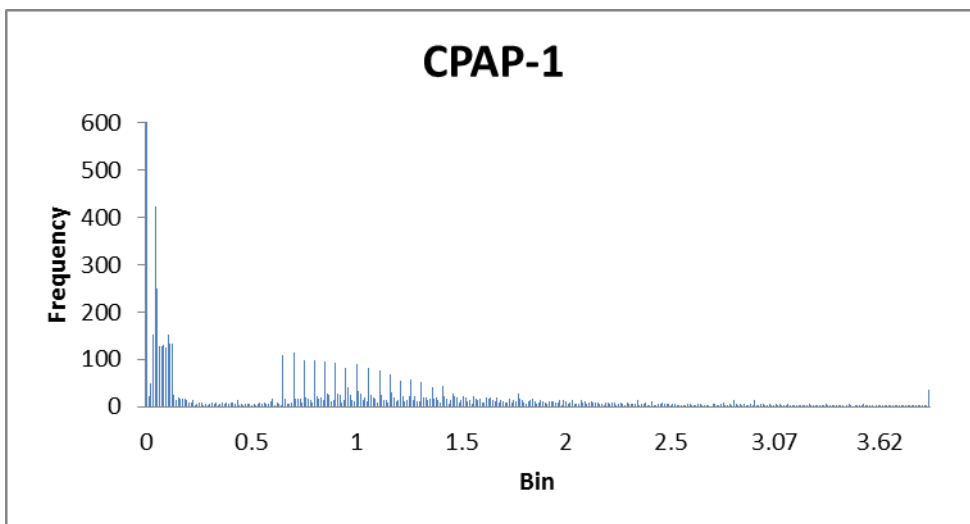
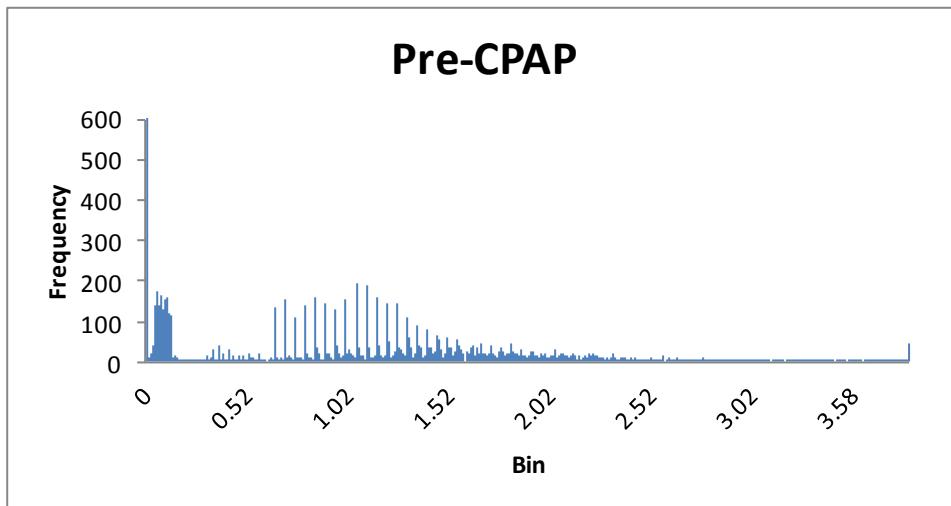


## Patient 12

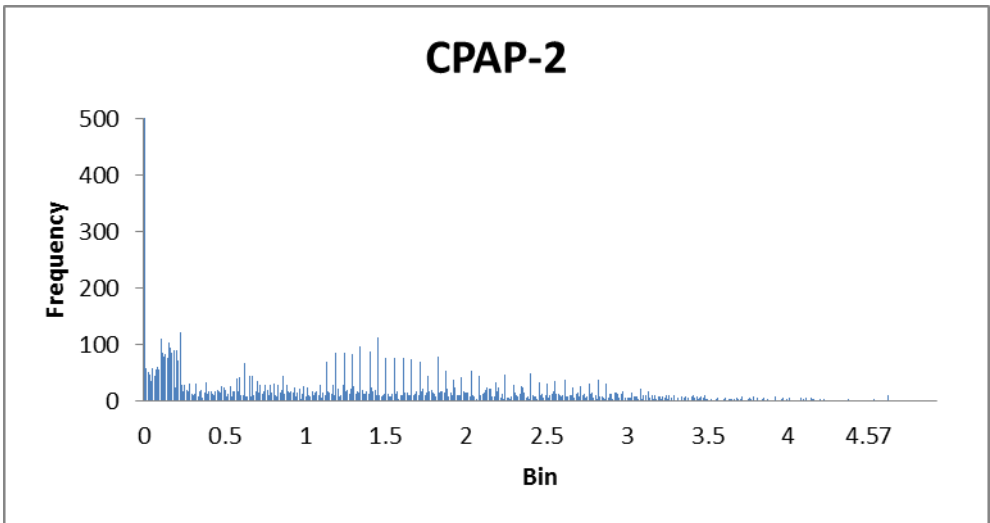
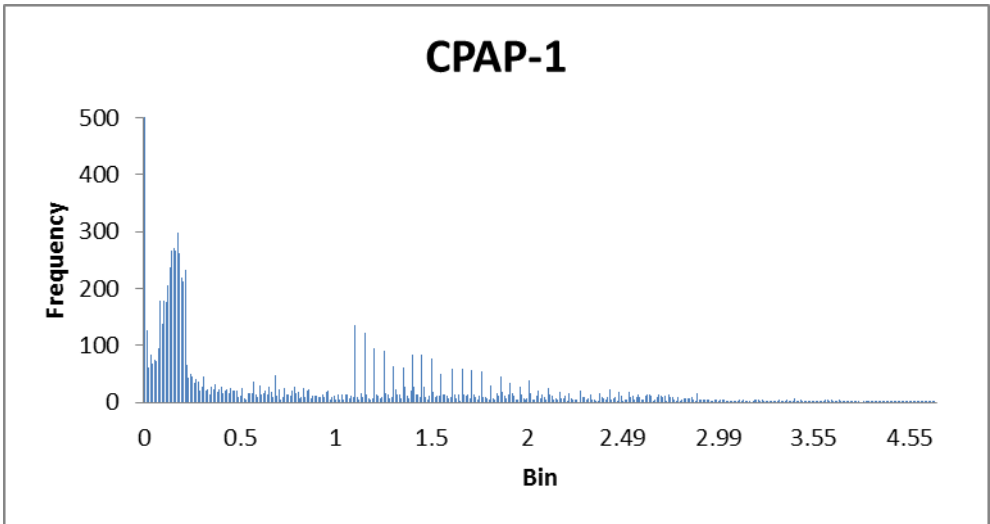
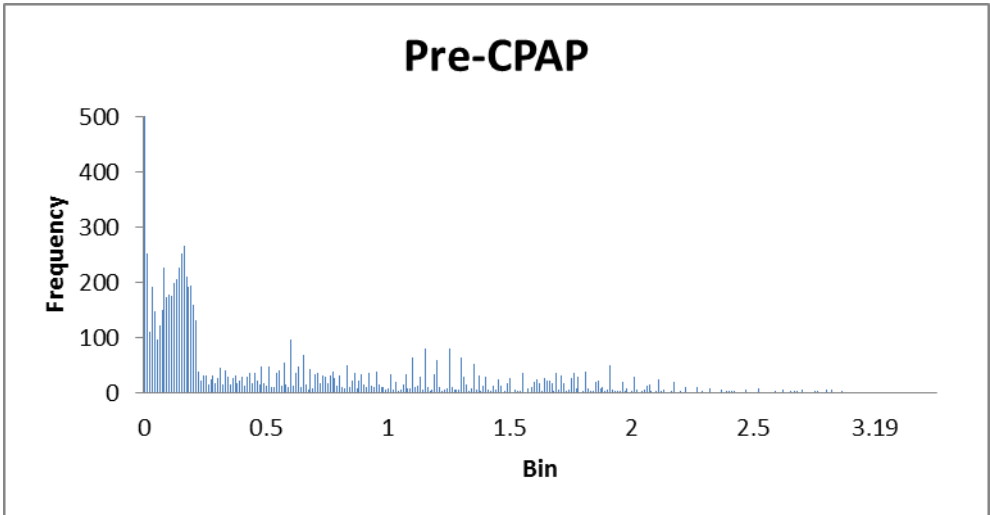


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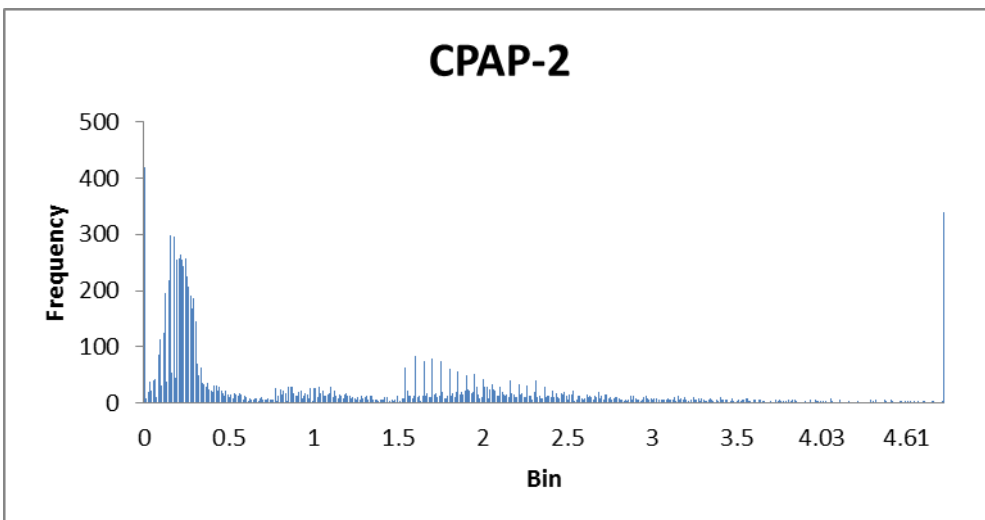
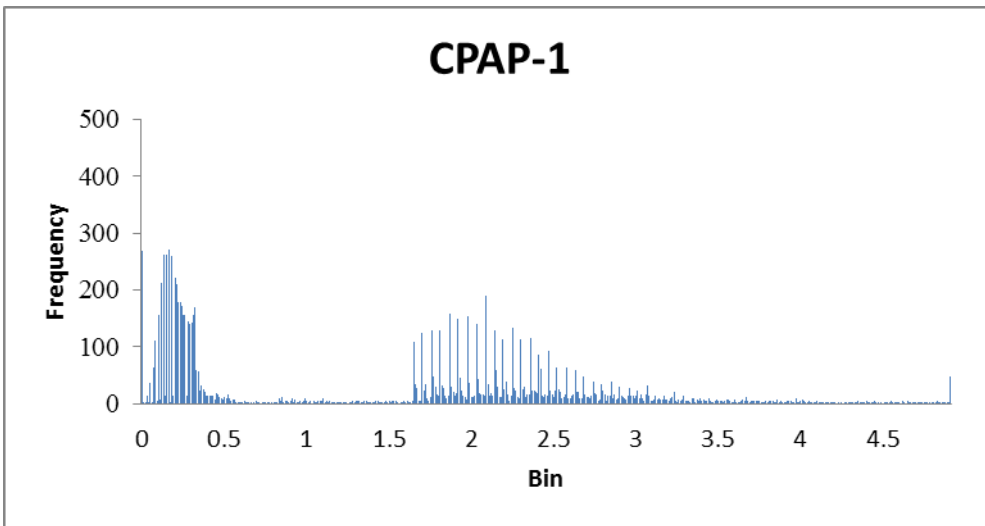
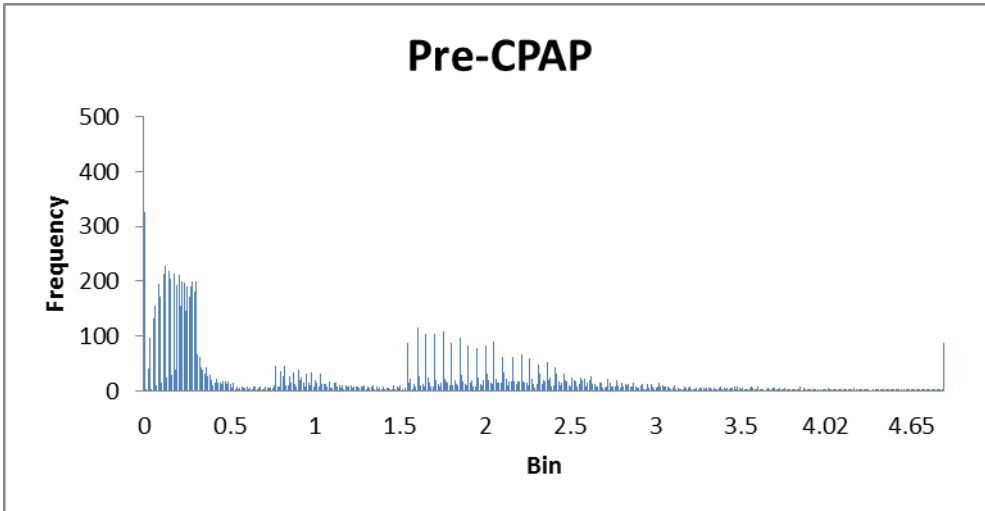
## Patient 1



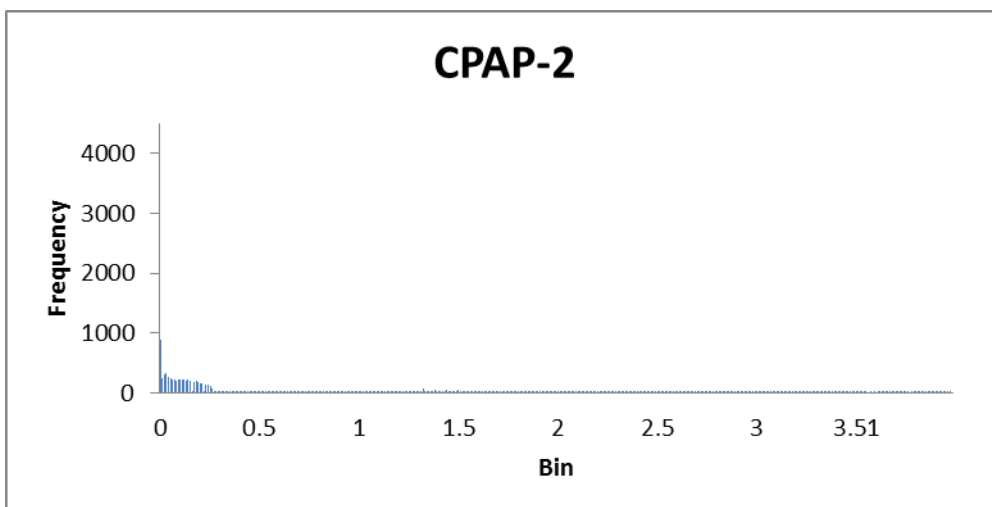
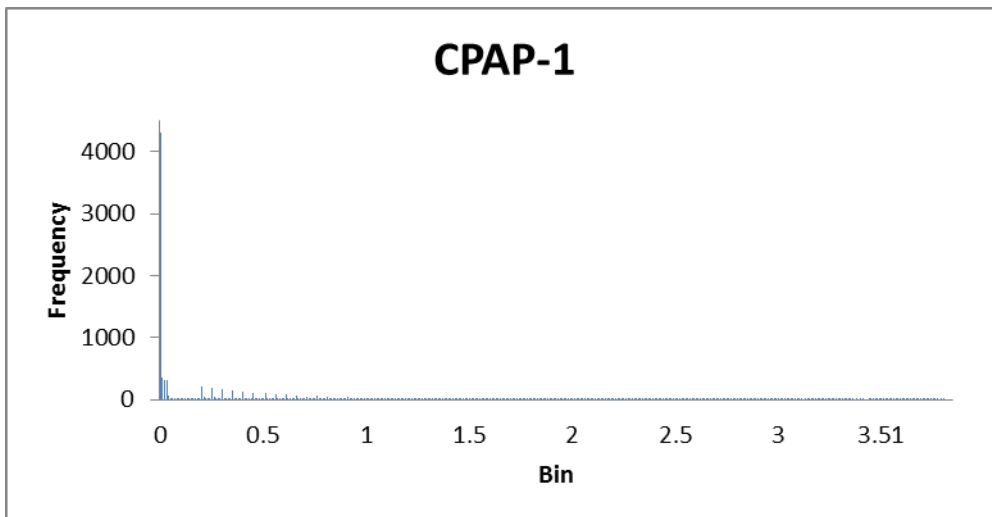
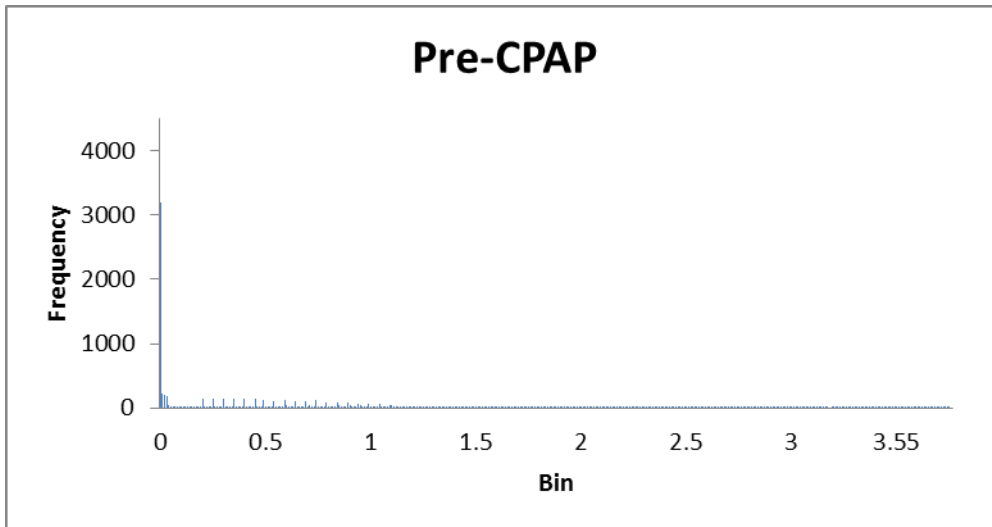
**Patient 2**



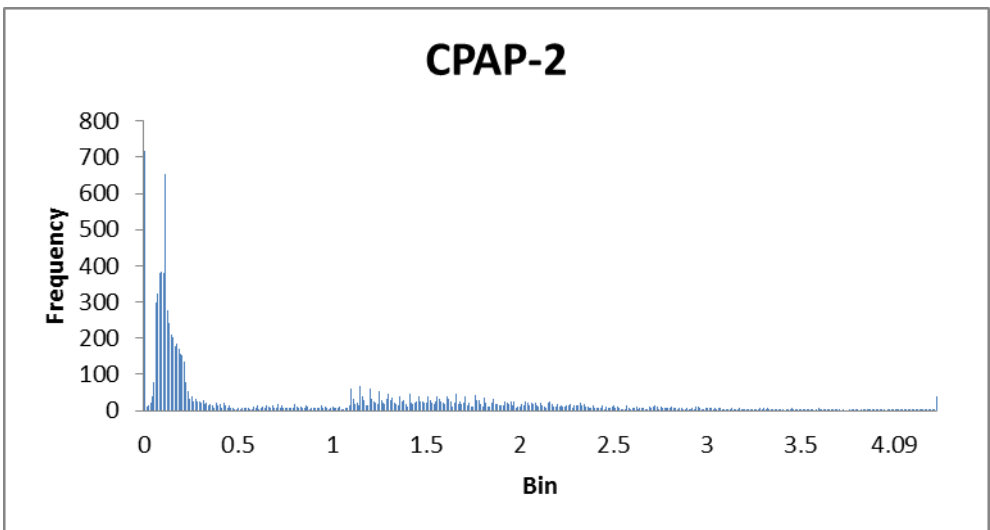
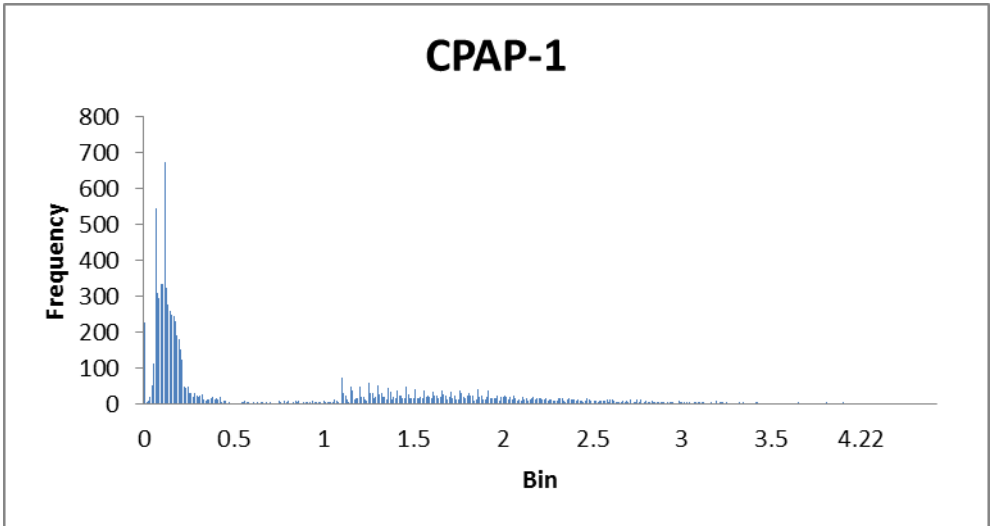
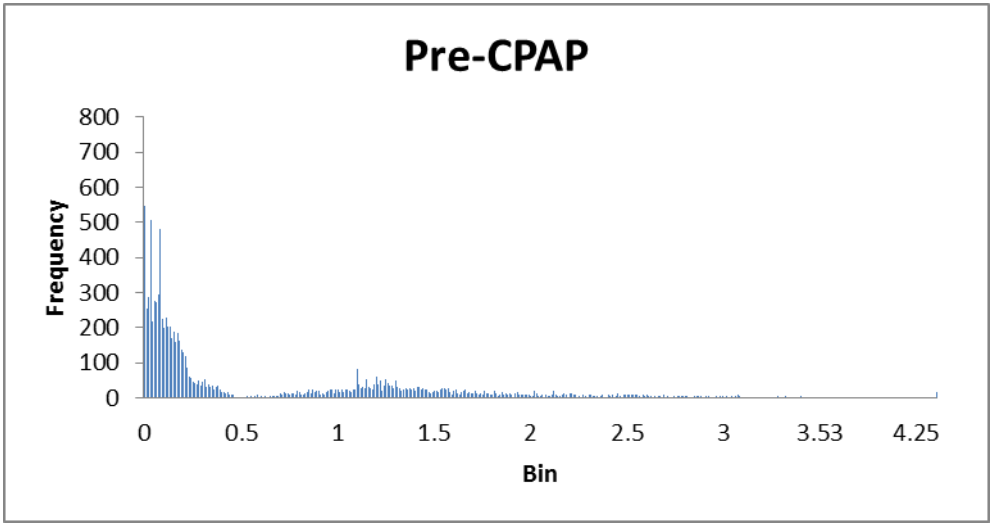
**Patient 3**



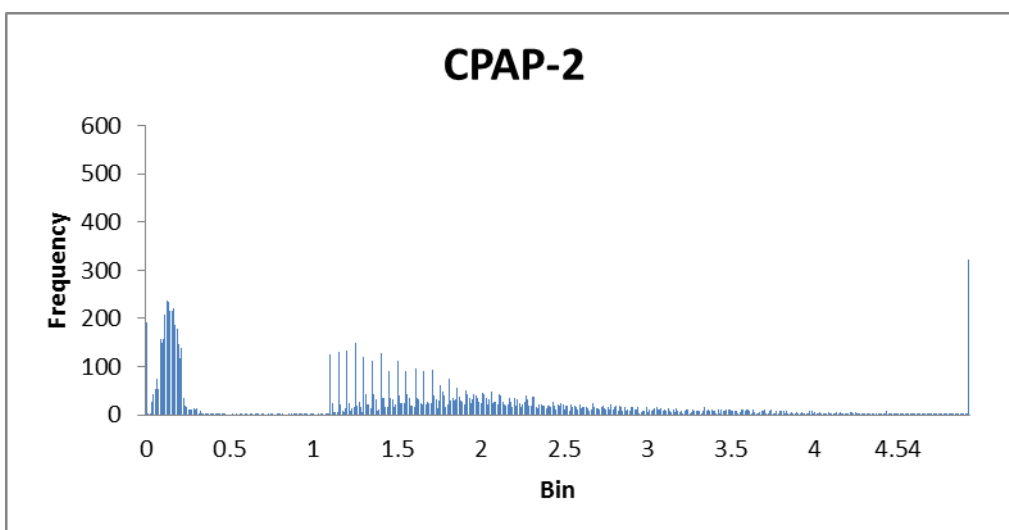
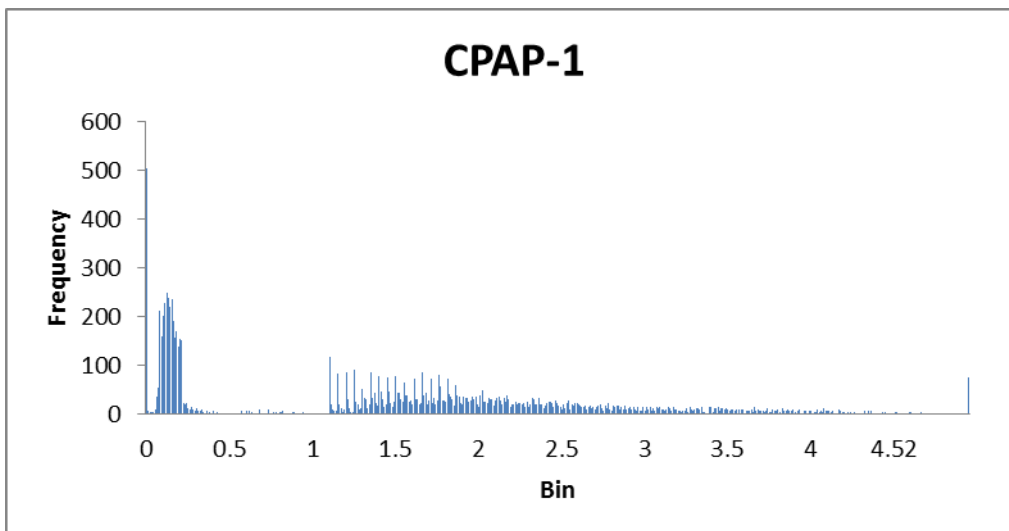
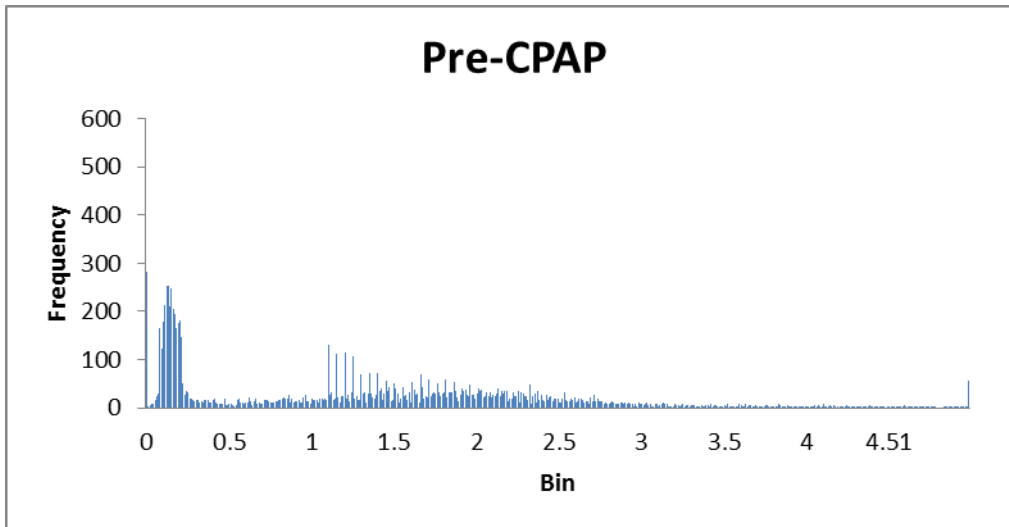


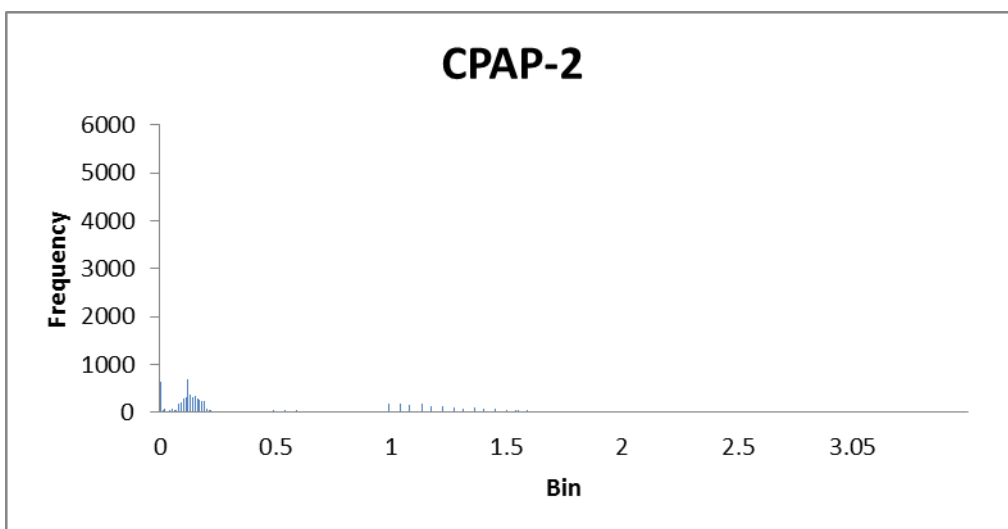
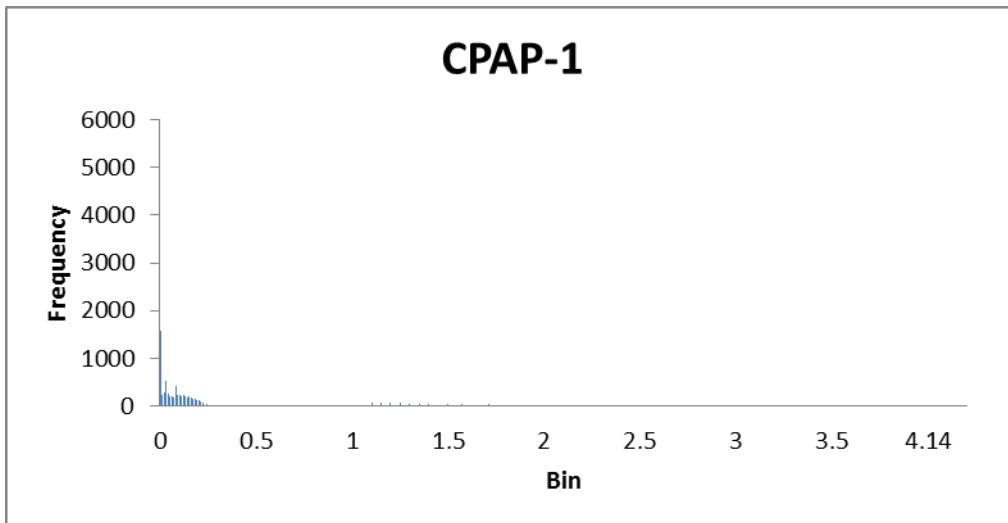
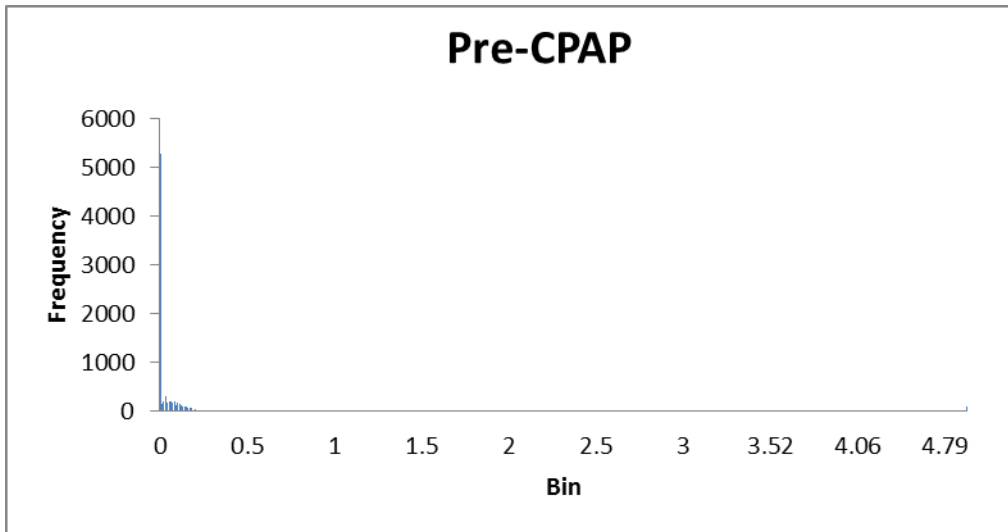
**Patient 4**

**Patient 5**

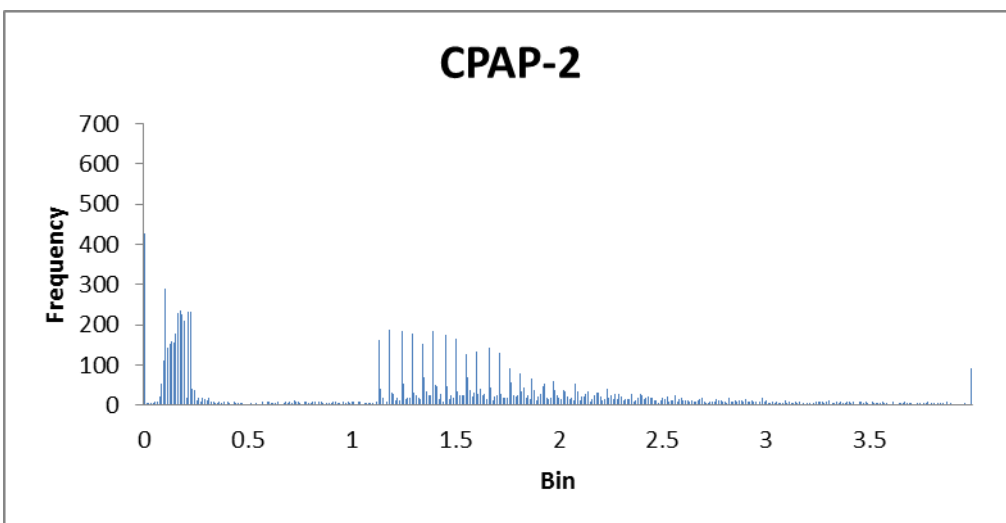
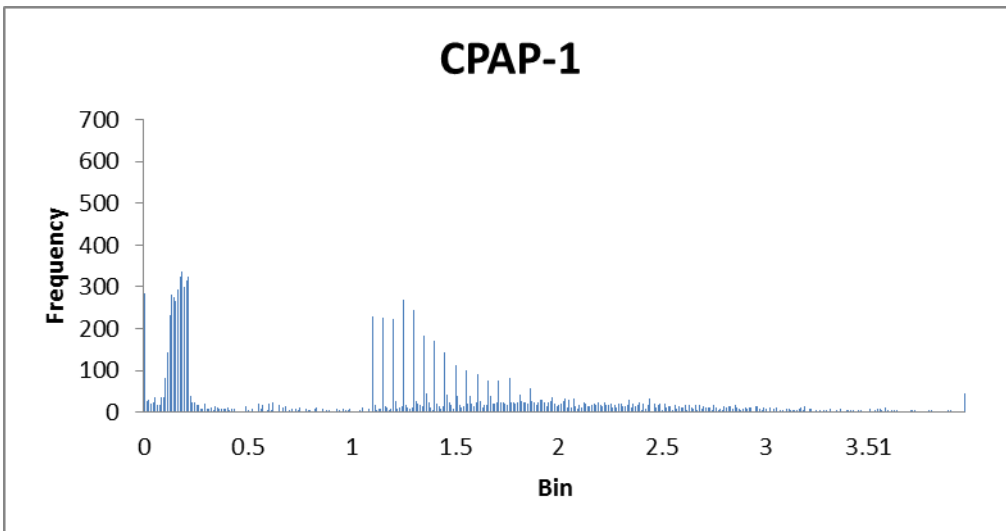
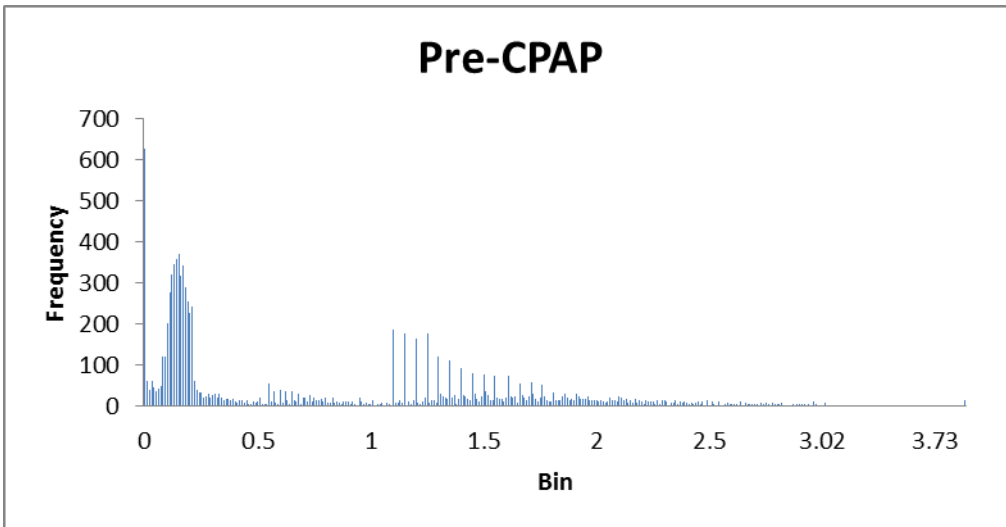


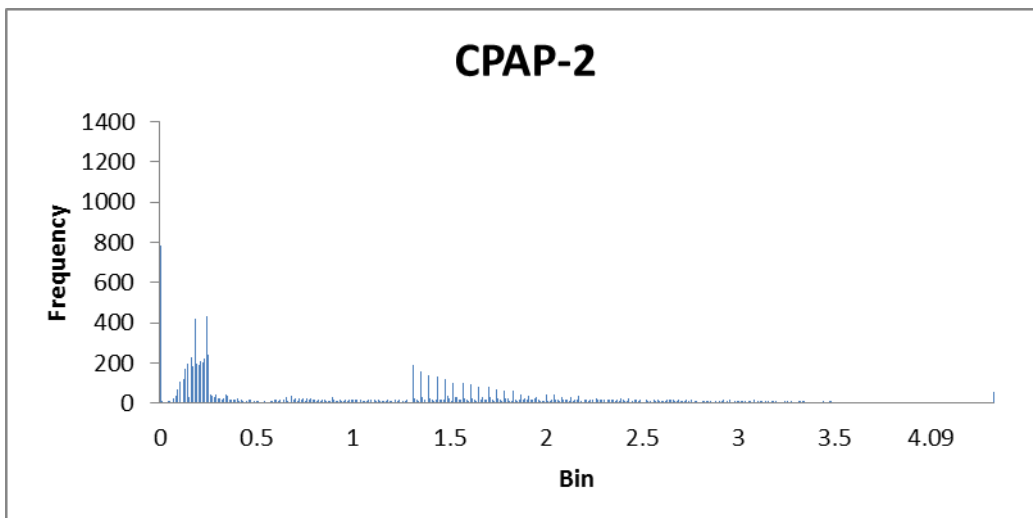
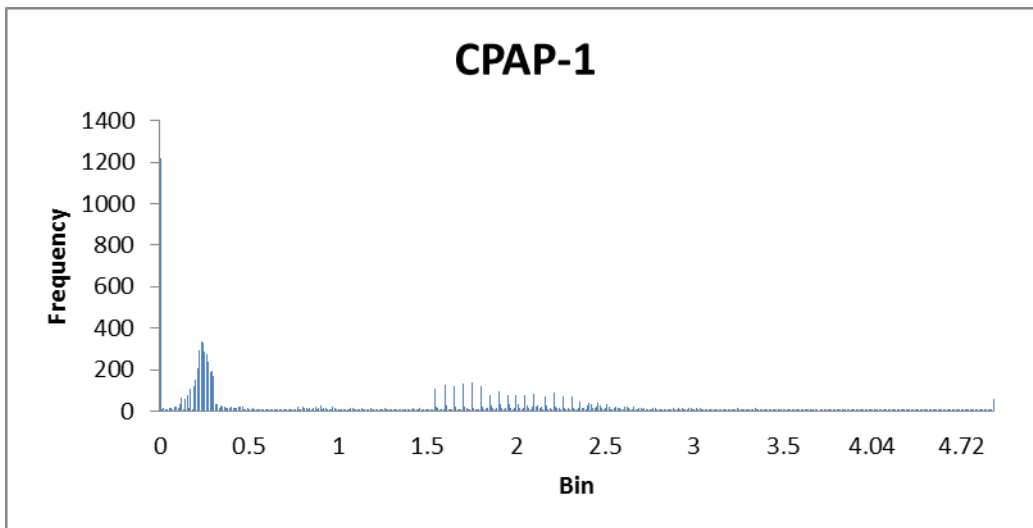
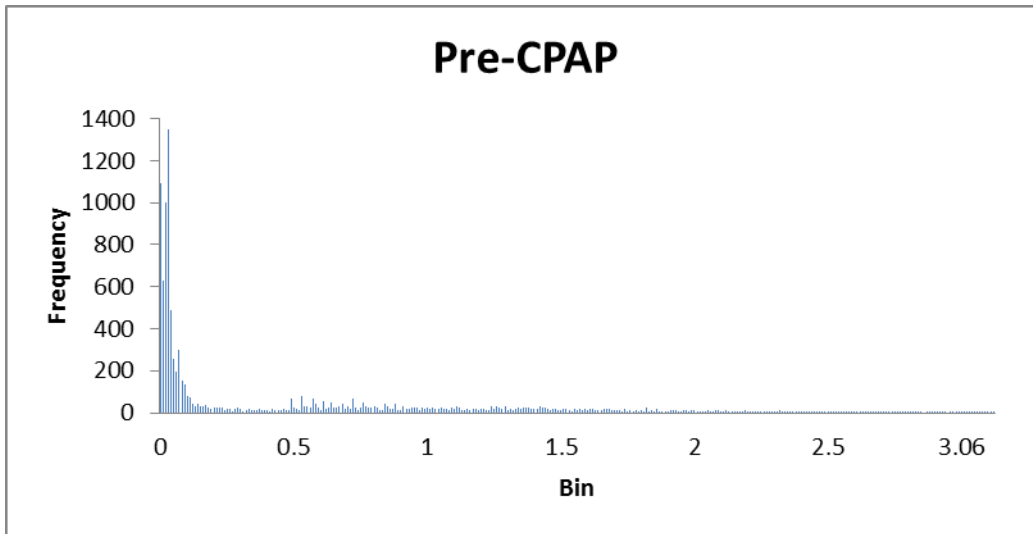
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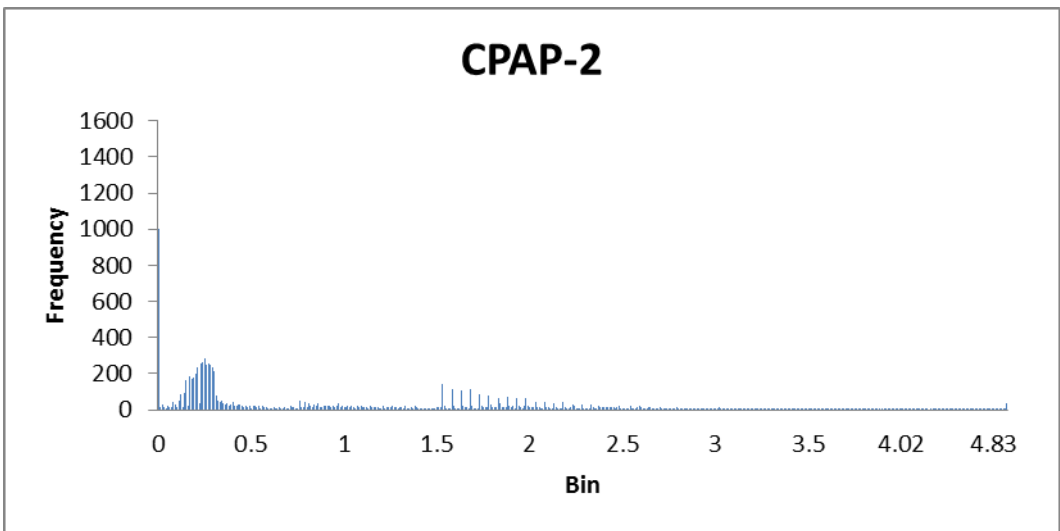
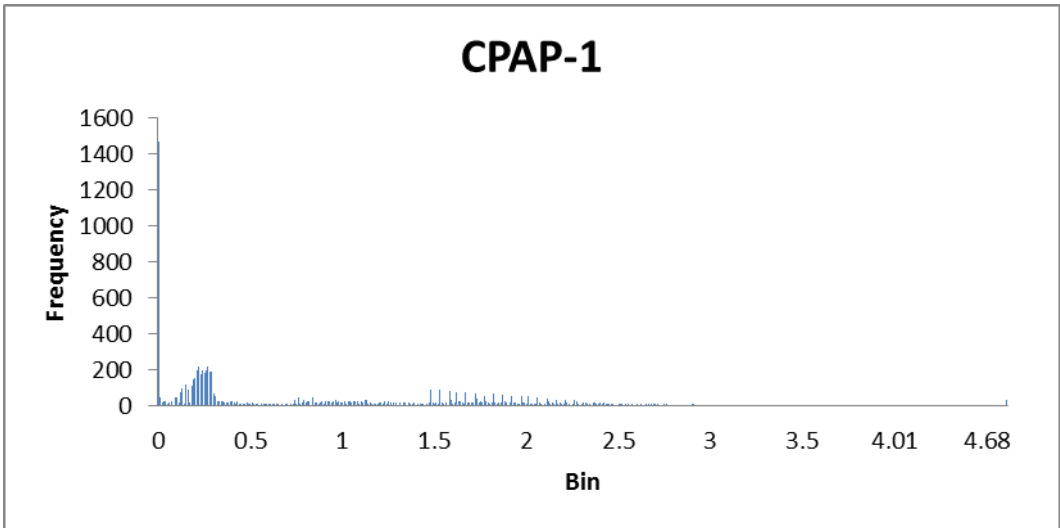
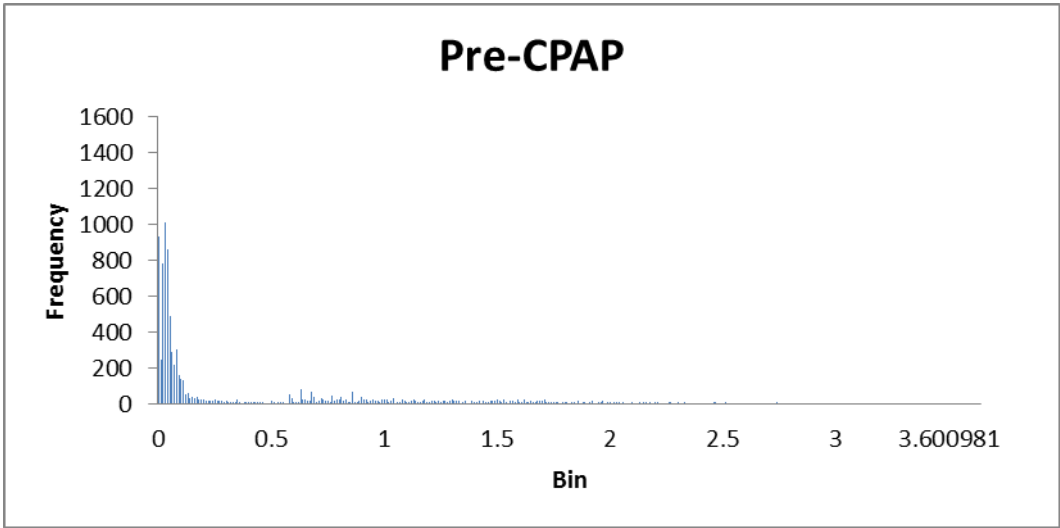
**Patient 7**

**Patient 8**

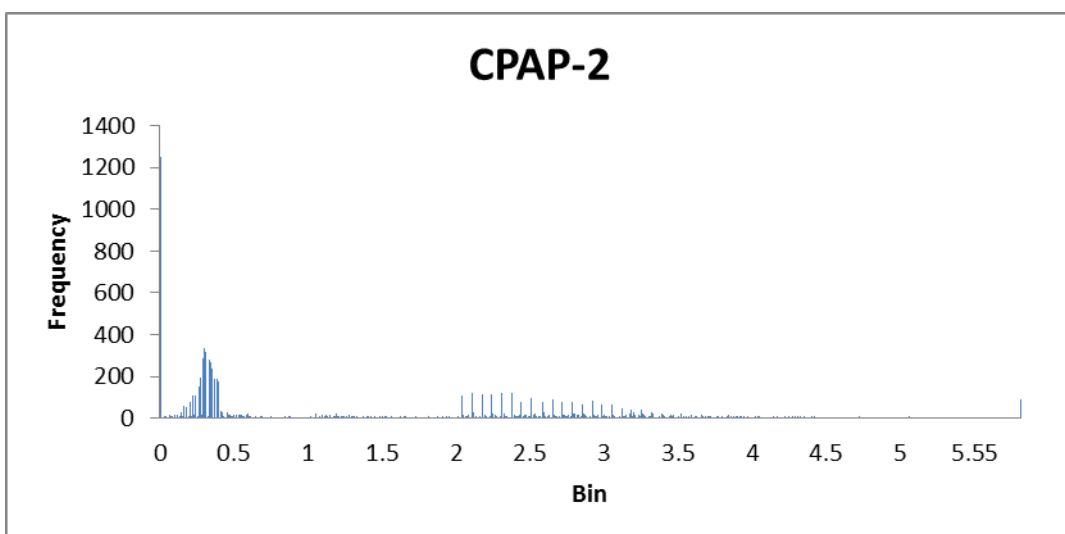
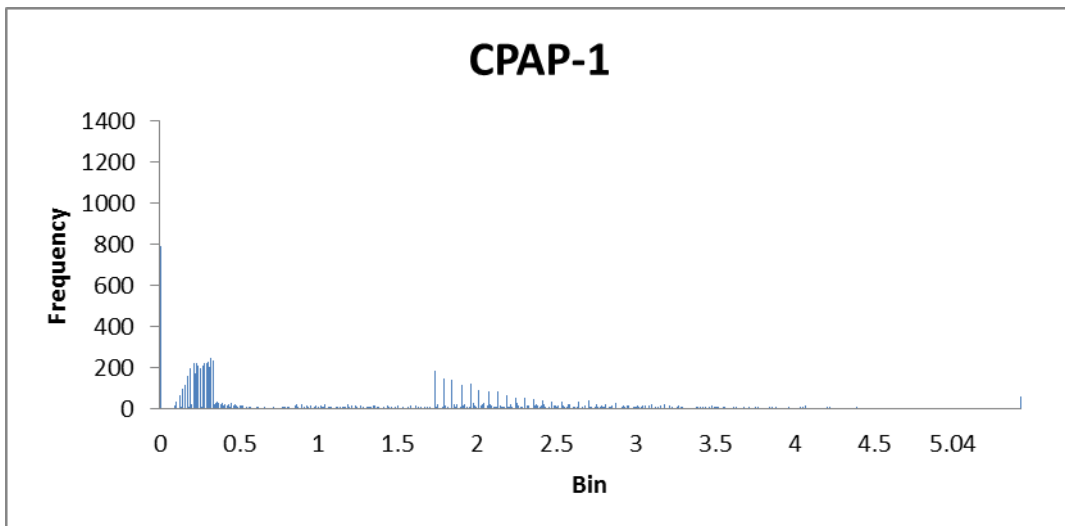
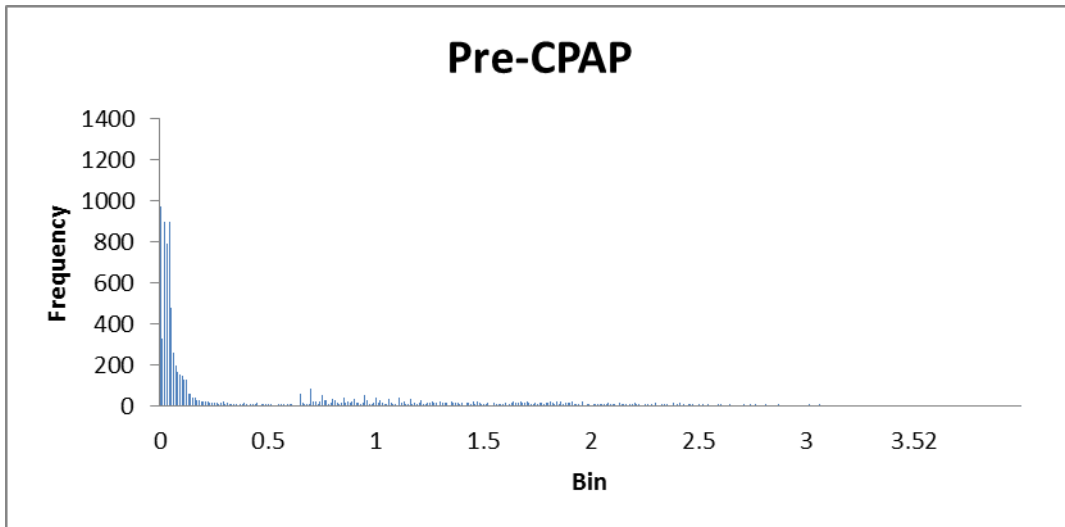


**Patient 9**

**Patient 10**



Patient 11





**Patient 12**

