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Resting energy expenditure using indirect calorimetry in individuals with moderate to low burns: A pilot study of associated factors, patient acceptability and comparison with predictive equations

Janica Bell
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**Resting energy expenditure using indirect calorimetry in
individuals with moderate to low sized burns: A pilot study of
associated factors, patient acceptability and comparison with
predictive equations**

By Ms Janica Bell

Supervisors: Associate Professor Philippa Lyons-Wall and Dr Angus Stewart

A report submitted in Partial Fulfilment of the Requirements for the Award of Bachelor of
Health Science, Honours, Faculty of Health, Engineering and Science, Edith Cowan
University.

Submitted December 2015

I declare that this thesis is my own work and does not include:

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Janica Bell
14th of December 2015

A/Prof Professor Philippa Lyons-Wall
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Abstract

Title: Resting energy expenditure using indirect calorimetry in individuals with moderate to low burns: A pilot study of associated factors, patient acceptability and comparison with predictive equations

Background: Energy expenditure increases following a burn injury. The extent of hypermetabolism is dependent on a range of factors including burn total body surface area. Moderate to low burn injuries (< 15% TBSA) represent majority of hospital admissions for burn injuries however, their energy expenditure remains unpublished. While indirect calorimetry (IC) is the gold standard for determining energy requirements, less accurate predictive equations are often used in practice. Acceptability of IC from a burn patient perspective has not been published.

Aim: To describe the resting energy expenditure (REE) of patients with a moderate to low burn injury using IC; compare measured REE to predictive equations; and determine the patient acceptability of IC.

Methods: Demographic, anthropometric and dietary data were collected for five male and three female burn patients. REE was determined using indirect calorimetry (Ultima CPX) and five predictive methods (Schofield, Harris-Benedict, Toronto and the Ireton-Jones equations, and energy-per-kilogram formulae). A written questionnaire assessed patient acceptability.

Results: Mean measured REE was 6494 ± 1625 kJ/day, lower than reported REE of major burn populations from the literature ($p < 0.05$). At a group level, the Schofield and Toronto equation were accurate to within $\pm 10\%$ of the measured REE with a mean difference of $5.21 \pm 12.16\%$ and $8.89 \pm 12.64\%$, respectively. At an individual level, the Schofield equation was accurate for 67% of participants and overestimated REE for 33% of participants. The Toronto equation was accurate for 50% of participants and overestimated REE for 50% of participants. IC was acceptable from a patient perspective with all participants willing to repeat the measure.

Conclusions: Results of this study support routine use of IC in moderate to low burn injuries, as it is acceptable to patients and avoids the inaccuracies of predictive equations. Where IC is not available, results suggest that the Schofield equation be used with caution to estimate REE for moderate to low burn injuries. Given the small sample size of this study, further research on the REE of moderate to low burn injuries is warranted.

Keywords: indirect calorimetry, resting energy expenditure, resting metabolic rate, burn, thermal injury, nutrition.

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14th of December 2015

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Chapter: Introduction and Background

1.1 Introduction

Burn injuries are associated with an increase in energy expenditure. If left untreated, this can lead to a loss of body mass resulting in an increased risk of morbidity and mortality (Ireton-Jones & Gottschlich, 1993). Accurate determination of energy expenditure and subsequent delivery of adequate nutrition are crucial for optimal recovery following a burn injury (Dickerson et al., 2002). Patients with moderate to low burn injuries represent the majority of burn-related hospital admissions within Australia (Burns Registry of Australia and New Zealand, 2014), yet their energy expenditure remains unpublished. This thesis will report the findings of a pilot study designed to describe and explore the energy expenditure of patients with moderate to low burn injuries using indirect calorimetry within the Western Australia (WA) State Adult Burn Unit. Relevant literature will be critically discussed with reference to the study hypotheses, research findings and study limitations. Recommendations for future research and clinical care of moderate burn injuries will be provided.

1.2 Background

Burn injuries are a serious global health problem which cause immediate trauma as well as long term physical, psychological and economic concerns for the individual and the community (World Health Organisation, 2008). A burn injury is defined as damage to the body tissue, typically the skin, secondary to exposure from flames, electricity, chemicals or radiation (Jeschke, Kamolz, Sjoberg, & Wolf, 2012). The most common cause of burn injuries are flames and scalds which account for 70% of burn-related hospital admissions in Australia (Burns Registry of Australia and New Zealand, 2014).

Burn injuries are the sixth leading cause of injury in Australia and are included in the National Health Priority Areas under Injury Prevention and Control (Pointer, 2013; Western Australia. Department of Health, 2009). It is estimated that burn injuries result in the loss of 10 million Disability Adjusted Life Years (DALYs) worldwide each year (World Health Organisation, 2008). They were estimated to account for \$84,887,000 in Australian health care expenditure between 2013 and 2014 (Australian Institute of Health and Wellness, 2015)

International data indicate that there were nearly 11 million burn injuries worldwide in 2004 (World Health Organisation, 2008). Global data suggest a downward trend in burn injuries and improvements in mortality rates for developed countries (Duke et al., 2011). In Australia, this is attributed to prevention initiatives including legislation of domestic smoke detectors and flame retardant sleepwear, as well as highly developed medical services for burn injuries (Duke et al., 2011; Harrison & Steel, 2006). However, burn injuries remain a severe type of trauma and continue to affect 1% of the Australian population each year, of which 10% require hospitalisation (Wasiak, Spinks, Clapperton, Cleand, & Gabbe, 2009). Recent data from the Burns Registry of Australia and New Zealand (2014) indicate that there were 1,700 adult burn injuries requiring hospital admission between 2013 and 2014. The rate of burn injury in WA is similar to that of other Australian states (Western Australia. Department of Health, 2009) with 336 admissions in 2013. Further analysis indicates that 87.5% of admissions in WA were for burn injuries < 10% TBSA and the highest incidence occurred in males aged 20 to 24 years at a rate more than double their female counterparts (Burns Registry of Australia and New Zealand, 2014; Duke et al., 2011).

Burn injuries range from minor, which do not require hospitalisation, through to major, which can result in death (Wasiak et al., 2009). Classification traditionally considers the extent and the depth of the injury. The 'rule of nines' is used in adult burn cases to determine the extent

of the injury (Baxter, Randall, & Kapur, 1953; Jeschke et al., 2012) and is reported as a percentage of total body surface area (TBSA) (*Figure 1*). Injuries affecting < 10% TBSA are considered minor, 10 to 20% TBSA are considered moderate, and > 20% TBSA are considered major (Morgan, Bledsoe, & Barker, 2000).

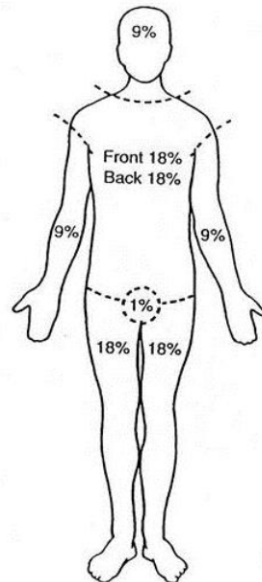


Figure 1. Rule of nines for the assessment of total body surface area in adults (Burns Registry of Australia and New Zealand, 2014)

The depth of the injury is classed as “superficial” where only the epidermis is involved; “partial” which involves the epidermis as well as varying levels of the dermis; or “full thickness” which involves both the epidermis and dermis as well as underlying muscle, bone, tissue or organs. This classification system replaces the previous “first”, “second” and “third” degree model (Mertens, Jenkins, & Warden, 1997). The WA State Adult Burn Unit applies a multifactorial method to classify burn injuries considering not only percentage TBSA and depth of burn but also age, presence of inhalation injury, burn location/s, presence of other injuries, psychosocial considerations and co-morbidities. Using this model, burn injuries are classified as minor, moderate or severe (Western Australia. Department of Health, 2009).

A multidisciplinary approach is applied to the treatment of burn patients with nutrition forming a crucial component (Mayes, Gottschlich, Khoury, & Warden, 1996; Rodriguez, Jeschke, Williams, Kamolz, & Herndon, 2011). Adequate and early nutrition has been shown to reduce mortality and morbidity in severe burn injuries through the maintenance of body weight, importantly lean muscle mass (Dickerson et al., 2002). Maintenance of lean muscle mass has been shown to improve wound healing, reduce mortality and reduce the risk of infective complications (Mendonça Machado, Gagnani, & Masako Ferreira, 2011; Rodriguez et al., 2011; Tredget & Yu, 1992). Following a burn injury there is a marked increase in resting energy expenditure (REE) which is referred to as hypermetabolism. The ability of the clinician to identify the extent of this hypermetabolism and match energy delivery is essential to successful nutrition management (Dickerson et al., 2002).

In a clinical setting, REE can be determined using either indirect calorimetry or predictive equations. Indirect calorimetry is considered more accurate, however, is limited by cost and equipment access. Therefore many clinicians rely on predictive equations, which have been shown to be inaccurate (Dickerson et al., 2002). Previous studies have focussed on the determination of energy needs for major burns due to the acuity and increased risk of mortality. However, moderate burn injuries, defined as $\leq 15\%$ TBSA, represent the majority of burn-related hospital admissions nationally and within WA. The limited evidence which is available indicates variation in the extent of hypermetabolism for moderate burn injuries and negative nutritional outcomes associated with inadequate nutrition delivery (Mancusi-Ungaro, Van Way, & McCool, 1992). This research study was undertaken to identify the REE of moderate burn injuries, describe the variables that are associated with REE, determine the accuracy of predictive equations used to estimate REE and the acceptability of indirect calorimetry measurements from the patient's perspective.

1.3 Literature Review

1.3.1 Energy expenditure

The energy required by humans for bodily functions is obtained from the environment through the consumption of food, specifically lipid, protein and carbohydrate. These energy substrates undergo oxidative reactions within the body producing carbon dioxide (CO₂), heat and the energy molecule adenosine triphosphate (ATP) (Ferrannin, 1988; Storey, 2004).

Total energy expenditure (TEE) has three components: the basal or resting metabolic rate; the thermic effect of feeding (TEF); and the thermic effect of activity (TEA) (Walker & Heuberger, 2009). The basal metabolic rate (BMR) is defined as the minimum rate of energy expenditure and is the energy used to maintain normal bodily functions such as organ systems (Owen, 1988). Combined, the brain and liver account for just 4 to 5% of total body weight however, they contribute to approximately 40% of the BMR reflecting their high energy needs (Owen, 1988). BMR is observed in subjects who are 12 hours post-absorptive in the early hours of the morning during deep sleep in a dim, quiet and thermo-neutral environment. Measurement conditions of BMR are difficult to attain and as a result, REE is frequently used in the clinical and research setting (Battezzati & Viganò, 2001; Owen, 1988; Schlein & Coulter, 2013). REE is measured in an awake but rested state rather than in a deep sleep. REE is approximately 10% greater than BMR reflecting the increase energy use in the awakened state (Matarese, 1997; Schlein & Coulter, 2013; Wooley & Sax, 2003). Measurement of REE requires individuals to be 12 hours post-absorptive and have abstained from intensive physical activity in the previous 12 hours. Testing should also occur in a dim, quiet and thermo-neutral environment and can be observed at any time of the day (Owen, 1988). REE is estimated to account for 65 to 70% of an individual's TEE (Battezzati & Viganò, 2001; Owen, 1988), as demonstrated in *Figure 2*.

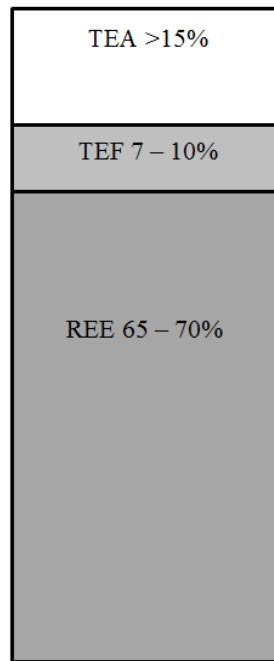


Figure 2. Components of total energy expenditure in healthy adults (Lee & Nieman, 2013)

Note. REE = resting energy expenditure; TEF = thermic effect of feeding; TEA = thermic effect of activity.

The TEF is the energy expended during nutrient metabolism and accounts for 7 to 10% of the TEE (Brandi, Bertolini, & Calafà, 1997; Lee & Nieman, 2013; Owen, 1988). As BMR and REE are typically measured in fasted subjects the addition of a 10% factor is recommended when determining TEE to account for the TEF (Ferrie & Ward, 2007). When measuring REE in a clinical setting, fasting may be contraindicated (e.g., in the critically ill patient) and measurements may be conducted in the fed state. In these instances, a factor for TEF should not be included in calculations for TEE as it has already been measured with the REE (Ferrie & Ward, 2007).

The TEA is the most variable component of TEE and is attributed to physical activity and muscular movement including fidgeting, shivering and purposeful activities such as sports (Walker & Heuberge, 2009). In sedentary adults TEA is approximately 15% of TEE. However,

this can increase to greater than 30% in highly active individuals (Poehlman, 1989). When determining TEE an activity factor should be applied to account for the energy expenditure associated with TEA, as demonstrated in **Table 1** (Ferrie & Ward, 2007).

It is well documented that REE is influenced by disease and injury (Long, Schafeel, Geiger, Schiller, & Blakemore, 1979; Walker & Heuberger, 2009). In 1979 Long et al. published their work quantifying the increase in energy expenditure observed during major sepsis, skeletal trauma, major thermal injury and a minor operation. The authors identified a 23% to 130% increase in REE within these groups (Long et al., 1979). Loss of heat, body tissues and fluids, fever and changes in metabolic hormones are responsible for the observed hypermetabolism (Ferrie & Ward, 2007). Long et al. (1979) and others (Barak, Wall-Alonso, & Sitrin, 2002; Elia, 2005) developed and recommended the use of injury factors which can be applied to REE or BMR to determine the TEE of injured and ill individuals (Ferrie & Ward, 2007). Such authors also proposed the application of an activity factor in determining TEE to account for the TEA in ill or injured individuals. However, the use of an activity factor for individual's with illness or injury is disputed, as despite an elevated REE, these populations frequently experience reduced mobility secondary to bed rest and sedation (Battezzati & Viganò, 2001; Elia, 2005; Ferrie & Ward, 2007). Royall, Fairholm, Peters, Jeejeebhoy, and Allard (1994) examined 24 hour energy expenditure in critically ill burn patients and found that 27.3% of TEE was attributed to activities such as wound dressings, patient agitation and physiotherapy, therefore proposing a 20% activity factor. However, in a randomised trial of indirect calorimetry directed feeding Saffle, Larson, and Sullivan (1990) reported that a 20% activity factor resulted in the overestimation of TEE.

Table 1

Method for determination of total energy expenditure in the ill or injured individual (Long et al., 1979).

$$\text{TEE} = \text{REE} \times (\text{activity factor}) \times (\text{injury factor}) \times \text{TEF}^{\text{a}}$$

^a Assumption that REE was determined in a post-absorptive state

Note. TEE = total energy expenditure; REE = resting energy expenditure; TEF = thermic effect of feeding

1.3.2 Energy expenditure in burn injuries

The elevated REE of individuals with a burn injury was initially described in the 1950s (Ireton-Jones & Gottschlich, 1993). This has been followed by an abundance of publications further investigating and quantifying the hypermetabolism observed within this population, as reviewed by Cunningham (1990). The metabolic response to a burn injury is considered biphasic with an initial ebb phase followed by a flow phase. The ebb phase occurs immediately after the injury and is characterised by reduced cardiac output, low oxygen consumption (VO_2), poor oxygen tissue perfusion, reduced glucose tolerance and lower REE (Herndon & Tompkins, 2004). The ebb phase lasts from two to five days (Herndon & Tompkins, 2004; Jeschke et al., 2011). Following the onset of the ebb phase, there is a gradual increase in VO_2 , cardiac output and REE, and an increased heart rate, thus signalling the beginning of the flow phase.

During the flow phases there is an increase in metabolic mediators such as catecholamines, cytokines including tumour necrosis factor (TNF) and interleukin-1 (IL-1) and glucocorticoids (Jeschke et al., 2011), as well as insulin resistance which results in augmented macronutrient metabolism (Tredget & Yu, 1992). Such metabolic mediators contribute to the amplification of protein breakdown and oxidation, illustrated by elevated urea levels, a flux of amino acids

in the fasted state and an increased protein oxidation rate of 1.2 g/kg/day compared to 0.85 g/kg/day in healthy individuals (Herndon & Tompkins, 2004; Tredget & Yu, 1992). Insulin resistance contributes to protein synthesis inhibition and promotes protein breakdown, resulting in a net protein catabolism which over time leads to a global loss of muscle mass (Tredget & Yu, 1992). Furthermore, insulin resistance results in hyperglycaemia which can increase an individual's risk for infective complications and fatty liver (Herndon & Tompkins, 2004; Masters & Wood, 2008; Tredget & Yu, 1992). Evidence indicates that lipid oxidation is increased by 132% in individuals with a burn injury, with lipids contributing the largest component of TEE at 72%. This is supported by the accelerated release of free fatty acid (FFA) from adipocytes which is observed post-burn injury (Herndon & Tompkins, 2004). However, a significant proportion of these FFAs are recycled back into triglycerides suggesting futile substrate cycling. This futile substrate cycling is also observed for glucose and protein and contributes to the elevated energy expenditure and results in muscle and adipose tissue wasting in the long term (Masters & Wood, 2008; Tredget & Yu, 1992).

Early publications reported that metabolism returned to healthy or pre-burn levels, following wound closure (Cunningham, Hegarty, Meara, & Burke, 1989; Saffle et al., 1985; Wilmore, Long, Mason, Skreen, & Pruitt, 1974). However, more recent literature has demonstrated that hypermetabolism may persist for months and even years beyond wound closure and is often referred to as a "hypermetabolic plateau" (Hart et al., 2000; Jeschke et al., 2011; Milner, Cioffi, Mason, McManus, & Pruitt, 1994; Noordenbos, Hansbrough, Gutmacher, Doré, & Hansbrough, 2000). Studies have demonstrated that patients with major burn injuries remain hypermetabolic at hospital discharge despite wound closure (Mancusi-Ungaro et al., 1992; Milner et al., 1994). By extrapolating from indirect calorimetry data on inpatients, Milner et al. (1994) reported that it would take 100 to 150 days to reach pre-burn metabolic rates for 20 to

40% TBSA injuries, and 250 days for > 70% TBSA injuries. Jeschke et al. (2011) found that hypermetabolism persisted for two years ($p < 0.05$) in children, with metabolic mediators, such as TNF, norepinephrine and interleukin factors, remaining elevated three years following the initial burn injury ($p < 0.05$). This is further supported by studies whereby early wound excision and grafting had no effect on the degree or length of hypermetabolism (Dickerson et al., 2002; Noordenbos et al., 2000). The time course of hypermetabolism for moderate burn injuries in adults has not been described in the published literature.

Early work by Wilmore et al. (1974) identified a positive correlation between hypermetabolism and burn injury TBSA, as illustrated in **Figure 3**. This association was confirmed by Saffle et al. (1985) and more recently by Jeschke et al. (2007) who reported a significant positive association between the degree of hypermetabolism and TBSA in children ($p < 0.05$). In adults, studies have identified the presence of a “hypermetabolic ceiling” (Saffle et al., 1985), whereby energy expenditure plateaus at approximately double the normal REE for burn injuries greater than 60% TBSA (Tredget & Yu, 1992). Evidence suggests that the “hypermetabolic ceiling” occurs when the maximal metabolic capacities of the respiratory and the circulatory systems are reached (Cunningham, 1990). Wilmore et al. (1974) identified that a higher room temperature was associated with a reduction in metabolic rate for burn injuries > 45% TBSA.

Despite an acceptance of the positive relationship between TBSA and hypermetabolism evident within the literature (Tredget & Yu, 1992) several studies have produced data that demonstrate inconsistencies (Mancusi-Ungaro et al., 1992; Noordenbos et al., 2000). Noordenbos et al. (2000) found no significant correlation between TBSA and hypermetabolism in an adult population. This is supported by Dickerson et al. (2002) who found no significant correlation between TBSA and REE in 24 male and female burn patients, with a TBSA injury ranging from 20 to 80% (NS).

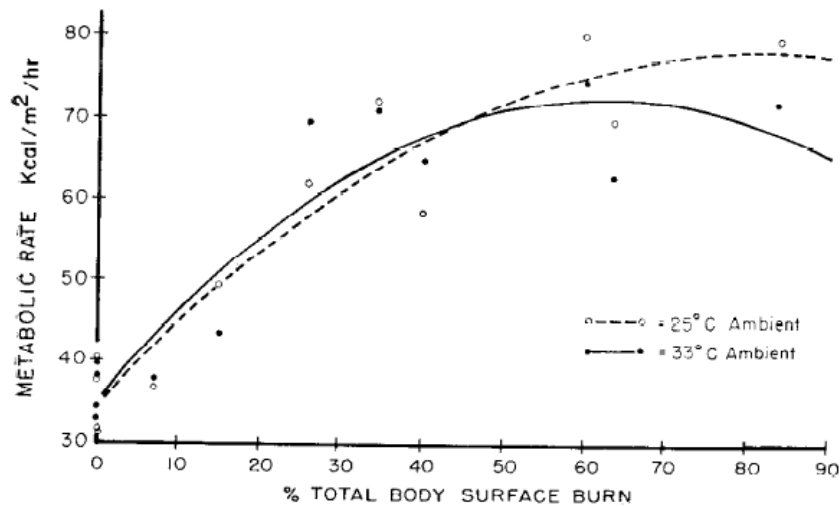


Figure 3 Correlation between metabolic rate (kcal/m²/hr) and total body surface area (%) following a burn injury at ambient temperature 25°C (dotted line) and 33°C (unbroken line) (Wilmore et al., 1974; Wilmore, Mason, Johnson, & Pruitt, 1975)

Variables other than TBSA, such as age, number of days post-burn injury, caloric intake and body temperature, have been shown to influence the REE of individuals with a burn injury to varying extents (Allard et al., 1988). In adult burn injuries, age has been reported as the second highest contributing factor to REE, following TBSA (Shields et al., 2013). However, other studies have reported no significant correlation between REE and age (Allard et al., 1990; Cunningham, 1980). The number of days post-burn injury has been shown to significantly correlate (r^2 not reported, $p < 0.001$) with measured REE (Allard et al., 1988). However, Milner et al. (1994) found no significant correlation ($r = -0.254$, $p = 0.072$) in the first 30 days following a burn injury and a significant correlation after 30 days ($r = -0.673$, $p < 0.001$). This is supported by Dickerson et al. (2002) who also did not find a significant correlation between post-burn days (NS) and energy expenditure. Calorie intake was shown as a significant variable

for energy expenditure by Allard et al. (1988) (r^2 not reported, $p < 0.001$). Cunningham et al. (1989) reported that body temperature was not correlated with REE, however, Allard et al. (1988) found a significant correlation (r^2 not reported, $p < 0.001$). The effect of these variables has been noted in a review by Cunningham (1990) who stated that the degree of hypermetabolism was the result of undefined interactions between several factors and reported a 30 to 40% variability in metabolism for the same TBSA burn injury. This is evident in a paper by Mancusi-Ungaro et al. (1992) who reported that some individuals with a TBSA $< 10\%$ had a REE equivalent or greater than those with a 50% TBSA burn injury. This led the authors to hypothesise that factors, other than TBSA, were determinants of the hypermetabolism observed following a burn injury (Mancusi-Ungaro et al., 1992; Yu, Wagner, Walesreswski, Burke, & Young, 1988). The inconsistent strength of correlation for these variables illustrates the individuality of each burn patient and the need for accurate methods to determine energy expenditure.

1.3.3 Determination of energy expenditure in burn injuries

The accurate determination of energy expenditure for individuals with a burn injury is crucial for the avoidance of over- and underfeeding (Moreira da Rocha et al., 2006; Prelack, Dylewski, & Sheridan, 2007). Overfeeding can lead to cardiopulmonary, hepatic and metabolic complications (Brandi et al., 1997; Prelack et al., 2007), whilst underfeeding can lead to increased risk of infections and poor wound healing (Rodriguez et al., 2011).

Indirect calorimetry is considered the gold standard for the determination of energy requirements in individuals with a burn injury (Berger, 2008; Rousseau, Losser, Ichai, & Berger, 2013) and international practice guidelines advocate for its routine use within this population (Rousseau et al., 2013). Indirect calorimetry measures oxygen and carbon dioxide

gas exchange to determine energy expenditure (Ferrannin, 1988; Walker & Heuberge, 2009). The development of portable bedside indirect calorimetry instruments in the 1980s has enabled clinicians to accurately and reliably measure REE, thus measuring the variation observed between individuals (Battezzati & Viganò, 2001; Ireton-Jones & Gottschlich, 1993; Moreira da Rocha et al., 2006). This allows clinicians to tailor the nutrition support regime to each patient's individual nutritional requirements and reduce the risks of under- and overfeeding (Wooley & Sax, 2003). Furthermore, indirect calorimetry is safe and non-invasive (Wooley & Sax, 2003). However, the high cost of the equipment combined with the time and training required to complete measurements have been inhibitory to its uptake in burn units (Campbell & Kudsk, 1988; Masters & Wood, 2008; Walker & Heuberge, 2009).

An alternative to indirect calorimetry is the use of predictive equations. Predictive equations are mathematical formulas developed using regression analysis of indirect calorimetry data collected on a cohort of subjects (Harris & Benedict, 1919; Ireton-Jones, Turner, Liepa, & Baxter, 1992). Equations may be developed within a healthy cohort and require an injury factor to account for the elevated REE associated with disease and injury; or developed with a cohort of ill subjects, such as burn patients, thereby incorporating the elevated REE into the equation and negating the need for an injury factor (Walker & Heuberge, 2009).

Predictive equations commonly include variables of influence on energy expenditure, such as age and weight. Predictive equations are favoured by clinicians as they are simple and quick, and overcome the financial and technical limitations of indirect calorimetry. For this reason, numerous predictive equations for burn patients have been developed (Cunningham et al., 1989; Dickerson et al., 2002). However, the inaccuracies of predictive equations are well recognised and international practice guidelines do not recommend their routine use for the determination of energy expenditure for patients with a burn injury as it may result in inaccurate

estimations of TEE and subsequent nutrition delivery (Shields et al., 2013; Walker & Heuberge, 2009).

1.3.3.1 Harris-Benedict equations

The seminal Harris-Benedict equations are considered the first attempt to develop a formula for the estimation of energy expenditure using analysis of BMR (Harris & Benedict, 1919; Moreira da Rocha, Alves, Silva, Chiesa, & da Fonseca, 2005; Walker & Heuberge, 2009). The equations were developed in 1919 with a cohort of 239 healthy adult male and female subjects with a mean age of 27 ± 9 years (Harris & Benedict, 1919). The original Harris-Benedict equations, which remain in use by clinicians today, are given in **Table 2**. An injury factor may be required when using these equations with hospitalised individuals to account for the increase in REE observed during disease and illness (Ferrie & Ward, 2007; Walker & Heuberge, 2009). For burn patients, these injury factors range from 20 to 220% with little consistency in recommendations (Cunningham, 1990; Dickerson et al., 2002; Masters & Wood, 2008; Wall-Alonso, Schoeller, Schechter, & Gottlieb, 1999). Historically, an injury factor of 200% has been common practice for patients with major burn injuries. However, this has been shown by multiple authors to overestimate REE in burn patients (Dickerson et al., 2002; Wall-Alonso et al., 1999). More recent publications suggest an injury factor range from 20 to 50% dependent on the TBSA (Australian and New Zealand Burn Association, 2007; Masters & Wood, 2008).

The Harris-Benedict equations are favoured by clinicians as they are easy to use, require only the variables of age, height and weight, and are frequently cited within the nutrition literature (Ferrie & Ward, 2007; Walker & Heuberge, 2009). However, the equations have been shown to both under and overestimate energy requirements when applied with an injury factor to

hospitalised individuals (Walker & Heuberge, 2009). Wall-Alonso et al. (1999) found the equations to overestimate, on average, by 16.5% when compared to indirect calorimetry in a burn injury cohort ($p < 0.05$). The inaccuracy observed with these equations, particularly the tendency to overestimate, is attributed to the methodology and equipment used in the original study. The original publication reports that BMR was measured however, the methodology reflects REE conditions in that subjects arrived on-site and were rested for 30 minutes prior to the testing (Harris & Benedict, 1919). In addition, the researchers used glass nasal tubes, rather than the modern face mask or canopy hood system to collect respiratory gas, which may have resulted in elevated energy expenditure secondary to agitation (Frankenfield, Muth, & Rowe, 1998). Furthermore, the equations are limited in their applicability as they were developed in young, healthy, fit Caucasian individuals which is not reflective of modern hospital patients, especially in relation to hypermetabolic states (Ferrie & Ward, 2007; Frankenfield et al., 1998).

Table 2

The Harris-Benedict equations for the estimation of resting energy expenditure in healthy adults (kcal/ day) (Walker & Heuberge, 2009)

Men	$REE \text{ (kcal/day)} = 66.47 + (13.75 \times W) + (5.0 \times H) - (6.76 \times A)$
Women	$REE \text{ (kcal/day)} = 655.1 + (9.56 \times W) + (1.85 \times H) - (4.68 \times A)$

Note. REE = resting energy expenditure; W = weight (kg); H = height (cm); A = age (years)

1.3.3.2 Schofield equations

The more recent Schofield equations are an extension of the work completed by the Food and Agricultural Organisation (FAO), World Health Organisation (WHO) and the United Nations University (UNU) (Ferrie & Ward, 2007), and are provided in **Table 3**. A cohort of 7000 healthy subjects from 23 different countries and 114 individual studies were used to develop the equations. The Schofield equations are popular among Australian clinicians as they form the basis for the calculation of the Estimated Energy Requirements (EER) in the Australian Nutrient Reference Value (NRVs) for healthy individuals and are thought to better reflect the Australian population (Ferrie & Ward, 2007). Despite the widespread use of the Schofield equations, they have been shown to overestimate energy expenditure in healthy and hospitalised individuals (Ferrie & Ward, 2007; Piers et al., 1997). Piers et al. (1997) found the Schofield equations to overestimate in healthy young Australian males by 406 kJ/day ($p < 0.001$) and females by 125 kJ/day ($p < 0.001$). Although statistically significant, the values may not be clinically relevant as weight balance studies suggest differences > 418 kJ/day are associated with long term weight change (Hasson, Howe, Jones, & Freedson, 2011). The accuracy of the equations is further questioned by reports of inconsistent temperatures during measurements for the original dataset leading to shivering or sweating which would have elevated REE (Ferrie & Ward, 2007). Despite the limitations of the equations, Masters and Wood (2008) found that they continued to be used in the estimation of energy requirements for burn patients with the addition of an injury factor ranging from 20 to 200% dependent on the TBSA. Lacking in the literature is a critique of the suitability of these equations for burn patients.

Table 3

The Schofield equations for the estimation of resting energy expenditure in healthy adults (MJ/ day) (Masters & Wood, 2008)

Men 18 – 30 years	$(0.063 \times W) + 2.896$
Men 30 – 60 years	$(0.048 \times W) + 3.653$
Men > 60 years	$(0.049 \times W) + 2.459$
Women 18 – 30 years	$(0.062 \times W) + 2.036$
Women 30 – 60 years	$(0.034 \times W) + 3.538$
Women > 60 years	$(0.038 \times W) + 2.755$

Note. W = weight (kg)

1.3.3.3 Ireton-Jones equations

The Ireton-Jones equations, originally published in 1992, were unique as they were developed and validated in a cohort of 200 critically ill trauma and burn patients, with 33% being ventilated (Ireton-Jones et al., 1992). The equations were revised in 1997 with 99 ventilated (42%) and 135 non-ventilated patients (58%). The revision enhanced the predictability of the ventilator equation with a reduction in the overestimation of energy requirements in 52 to 65% of subjects but did not improve the predictability of the non-ventilator equation and therefore no revisions were made to this formula (Ireton-Jones & Jones, 2002). The revised equations are provided in **Table 4**.

Table 4

The revised Ireton-Jones equations for the estimation of resting energy expenditure in critically ill adults (kcal/ day) (Ireton-Jones & Jones, 2002)

Non-ventilated	$629 - (11 \times A) + (25 \times W) - (609 \times O)$
Ventilated	$1784 - (11 \times A) + (5 \times W) + (244 \times S) + (239 \times T) + (804 \times B)$

Note. A = age (years); W = weight (kg); O = body mass index > 27 kg/m² (1 = present; 0 = otherwise); S = gender (1 = male; 0 = otherwise); T = trauma (1 = present; 0 = otherwise); B = burns (1 = present; 0 = otherwise)

Unlike the Harris-Benedict and Schofield equations, the Ireton-Jones equations do not require the use of an injury factor. This, and their more recent publication which reflects current medical interventions, are strengths of the equations (Ferrie & Ward, 2007). However, studies have found the equations to vary in accuracy from 28 to 83% of measured REE dependent on the population (Walker & Heuberger, 2009). The equations have been found to perform most accurately in a younger obese population of mixed critically ill patients (Walker & Heuberger, 2009). In a burns population, the original equations have been shown to lack precision with a 20% mean error for the ventilated equation and a 30% mean error for the non-ventilated version when compared to measured REE using indirect calorimetry (Dickerson et al., 2002). The equation for ventilated patients assumes the same severity for all burn injuries (Ferrie & Ward, 2007) which may account for the error observed by Dickerson et al. (2002). Despite the limitations, these equations continue to be used to estimate energy expenditure for individuals with a burn injury (Masters & Wood, 2008).

1.3.3.4 Toronto equation

The Toronto equation has been developed specifically for burn patients using a cohort of 23 male and female ventilated and non-ventilated burn patients for a total of 155 indirect calorimetry measurements (Allard et al., 1988). The mean TBSA for the cohort was 39.2% (range of 7 – 90%) with a distribution of participants across the TBSA range (7 for 7 – 19% TBSA; 6 for 20 – 39% TBSA; 3 for 40 – 59% TBSA; and 7 for > 60% TBSA). As with the Ireton-Jones equations, an injury factor is not required. The equation is provided in **Table 5**.

Table 5

The Toronto equation for the estimation of resting energy expenditure in adult burn patients (kcal/ day)(Allard et al., 1988)

$$-4343 + (10.5 \times \%TBSA) + (0.23 \times CI) + (0.84 \times EBEE) + (114 \times T) - (4.5 \times PBD)$$

Note. %TBSA = % of total burn surface area; CI = calories received in the previous 24 hours; EBEE = estimated basal energy expenditure using the Harris-Benedict equations; T = average hourly body temperature for the previous 24 hours (°C); PBD = post burn days.

The authors of the Toronto equation found that TBSA, caloric intake and predicted REE using the Harris-Benedict equations were significantly associated with measured REE (all $p < 0.001$), as were body temperature and days post-burn injury (both $p < 0.01$). Therefore these variables were incorporated into the predictive equation using stepwise multiple regression analysis. The number of surgical grafting interventions was not significantly correlated with measured REE and was therefore not included in the formula (Allard et al., 1988). The resulting equation correlates well with measures of REE using indirect calorimetry ($r = 0.82$, $p < 0.001$) (Allard et al., 1988). This has also been observed by Tancheva et al. (2005), Royall et al. (1994) and

Wall-Alonso et al. (1999) who found no significant difference between the Toronto equation and measured REE using indirect calorimetry in adult burn patients.

In contrast, Garrel and de Jonge (1993) observed that the equation underestimated by 24% when applied to ventilated adult burn patients. Dickerson et al. (2002) found the equation to underestimate in a cohort of 24 patients with a TBSA 20 to 80% ($p = 0.001$). Despite these limitations, the Toronto equation continues to perform as one of the more accurate and reliable equations for burn patients. Furthermore, it is applicable to both ventilated and non-ventilated patients and a wide range of TBSA injuries due to the population in which it was developed (Allard et al., 1990). However, the equation is limited by its complexity and the ability to obtain the variables required for the calculation (Masters & Wood, 2008; Rodriguez et al., 2011).

1.3.3.5 Energy-per-kilogram equations

An alternative to the mathematically derived predictive equations are the energy-per-kilogram of body weight equations, given in **Table 6**. Yu et al. (1988) first described this method by observing that 12 severely burnt patients had a mean energy expenditure of 130 kJ/kg/day. This method was later popularised by the American College of Chest Physicians for all critically ill patients (Walker & Heuberge, 2009). Other than the early work by Yu et al. (1988) little has been published or validated regarding this method in burn populations. Berger (2008) and Dickerson et al. (2002) both refer to the formula as “common practice” with no source available. An analysis by Dickerson et al. (2002) evaluated three energy-per-kilogram formulae and found that none were precise. The mean error was 23%, 23% and 27% for the 130 kJ/kg/day, 146 kJ/kg/day, and 167 kJ/kg/day, respectively, where imprecision was defined as

> 15% of the measured REE using indirect calorimetry. The 167 kJ/kg/day was shown to overestimate energy requirements by $2,675 \pm 3,711$ kJ/day (Dickerson et al., 2002)

Table 6

The energy-per-kilogram equations for the estimation of resting energy expenditure in adult burn patients (kJ/day) (Berger, 2008)

TBSA < 40%	125 – 146 kJ/kg/day
TBSA > 40%	146 – 210 kJ/kg/day

1.3.3.6 Summary

All predictive equations have been shown to have a clinically relevant degree of inaccuracy when compared to indirect calorimetry, including both the over- and underestimation of energy requirements (Dickerson et al., 2002). Despite this, predictive equations remain widely used. This is attributed to the high cost associated with purchasing and maintaining indirect calorimetry equipment and the comparative simplicity of the predictive equations (Rodriguez et al., 2011; Rousseau et al., 2014). Results of surveys conducted in Europe (Rousseau et al., 2014), North America (Graves, Saffle, & Cochran, 2009) and Australia (Masters & Wood, 2008) found that 100% of burn centres continue to use predictive equations despite 30% of these centres in Europe, 66% of these centres in North America and 40% of these centres in Australia having access to indirect calorimetry. One limitation of current predictive equations for burn patients is that all have been developed and validated in populations with a mean TBSA classified as major, which is > 20% TBSA. No equation has been designed for use with moderate burn injuries and validation of existing equations for moderate burn injuries is

lacking. Currently the WA State Adult Burn Unit determines energy expenditure by calculating both the Schofield and Toronto equations and taking a mean value. Using clinical experience, the dietitian will make calorie delivery adjustments to account for loss of weight, infection, repeated surgeries and wound healing (M. Cork, personal communication, March 1, 2016).

1.3.4 Patient acceptability of indirect calorimetry

While previous studies have evaluated the techniques required for indirect calorimetry in burn and critically ill patients (Moreira da Rocha et al., 2006; Wooley & Sax, 2003) no published studies, to the researcher's knowledge, have considered the acceptability of indirect calorimetry as assessed by the patient. Several studies have investigated the experiences of staff performing the measurement. One study reported that indirect calorimetry measurements took an average of 35 minutes and concluded that this was feasible for a clinical setting (De Waele et al., 2013). Another study identified that indirect calorimetry measurements were limited by the availability of trained staff resulting in poor compliance with unit protocols (Charriere, Delodder, & Berger, 2013). Both studies were conducted with ventilated patients and were not specific to burn patients. A survey conducted by Campbell and Kudsk (1988) found that 41% of hospitals who owned an indirect calorimeter did not routinely use the measures to guide delivery of nutrition. Barriers cited in this study included incompatibility between the indirect calorimeter and ventilators and difficulties in calibration. Since this publication, indirect calorimeter equipment and techniques have improved and become accepted as part of routine assessment for many, but not all, burn centres (Holdy, 2004). An understanding of the patient experience in terms of measurement duration, comfort during measures, acceptability of equipment, and ability of the patient to follow the procedures is yet to be elicited for all patients including those with burn injuries.

1.4 Research aims

The aims of this study were to describe the REE of moderate size burn injuries, defined as 5 to 15% TBSA, using indirect calorimetry; compare the measured REE of this cohort to published predictive equations; and determine the acceptability of indirect calorimetry measurements from a patient perspective.

1.5 Research questions

1. How does resting energy expenditure of a moderate burn injury, determined using indirect calorimetry, compare to the energy expenditure of larger burn injuries, determined using indirect calorimetry, as reported in previous published studies?
2. How does resting energy expenditure change over time for a moderate burn injury (i.e., 72 hours after admission, after surgery or 1 week post-admission, and 6 weeks after admission)?
3. Is there an influence of multiple variables¹ on the resting energy expenditure of a moderate burn injury?
4. Do the published predictive equations accurately estimate resting energy expenditure of moderate burn injuries?
5. Is indirect calorimetry an acceptable² tool from the patient perspective to measure the resting energy expenditure following a moderate burn injury?

¹Variables include: age, gender, body mass index (BMI), hand grip strength (HGS), Patient Generate-Subjective Global Assessment (PG-SGA) score, total body surface area (TBSA) burn injury, post-burn days

²Acceptability will be measured using a written questionnaire.

1.6 Hypotheses

1. The measured resting energy expenditure of patients with a moderate burn injury (defined as 5 to 15% total body surface area) will be significantly less than that of patients with a major ($\geq 15\%$ total body surface area) burn injury from published studies.
2. The measured resting energy expenditure of patients with a moderate burn injury will significantly decrease within 6 weeks of the burn injury.
3. Patients with a moderate burn injury of older age, female gender, poorer nutritional status (reduced hand grip strength, higher PG-SGA score or underweight body mass index) or less severe burn injury (lower total body surface area or burn thickness) will have a significantly lower resting energy expenditure than patients of a younger age, male gender, adequate nutritional status (hand grip strength, lower PG-SGA score or body mass index within healthy ranges), or more severe burn injury (higher total body surface area or burn thickness).
4. The estimated resting energy expenditure from selected¹ published predictive equations in patients with moderate burn injuries will be accurate to within $\pm 10\%$ of the measured resting energy expenditure using indirect calorimetry.
5. All patients with a moderate burn injury will report that the method of indirect calorimetry measurements is acceptable in terms of test duration and timing, comfort, privacy and willingness to repeat the measurement.

¹ The Schofield, Harris-Benedict, Toronto and Ireton-Jones equation, and the 100 – 125 kJ/kg/day energy-per-kilogram formulae

Chapter: Methodology

2.1 Design

This is a single-centre observational pilot study employing quantitative analysis to identify and explore the determinants of resting energy expenditure (REE) in individuals with a moderate burn injury. Indirect calorimetry was used to measure REE in the cohort and additional anthropometric, medical and dietary data were collected to enable analysis of the variables of influence on REE. A written questionnaire was undertaken to explore the participant experience during the indirect calorimetry measurements.

2.2 Participants

Participants were recruited from the Western Australian (WA) State Adult Burn Unit located at Fiona Stanley Hospital (FSH) between the 11th of March 2015 and the 31st of July 2015. All patients with a total body surface area (TBSA) burn injury between 5 and 15% were screened for eligibility between the 11th of March and the 30th of June. From the 1st of July until the 31st of July the criterion was amended to < 15% TBSA to increase the number of participants, with the aim to recruit a total of 30 participants for the study. This study had approval from the Edith Cowan University (ECU) Human Research Ethics Committee (HREC) and the FSH HREC (ECU 11916 and FSH 14-122).

Patients were excluded if they were < 18 years of age; required supplemental oxygen or were ventilated; had a non-thermal burn injury (e.g., an electrical or chemical burn); had an inhalation burn injury; had a head injury; had a facial burn injury or other trauma which inhibited the use of a face tent for the indirect calorimetry measurement; or were being treated with dialysis or fluid resuscitation. These exclusion criteria were applied to obtain a

homogenous study population secondary to the small sample size thus reducing potential confounding factors. Ventilated patients were beyond the scope of the study and patients receiving dialysis treatment, fluid resuscitation and supplemental oxygen were excluded due to potential error with indirect calorimetry measurements (Compher et al., 2006; McClave & Snider, 1992).

2.3 Materials

2.3.1 Demographic characteristics

Participant demographic data were collected from the FSH electronic medical notes systems, Burns Information Management System (BIMS) (FSH Adult Burn Unit, Western Australia). This information included age; gender; depth of burn injury reported as superficial, superficial partial, partial, deep partial and full thickness; extent of burn injury reported as TBSA; burn agent; and data and time of burn injury occurrence.

Current medications were sourced from the bedside nursing notes after each indirect calorimetry measurement and were examined for their influence on REE. The online pathology system, iSOFT (CSC, Australia) was used to obtain biochemical data which was compared to reference ranges and examined for the presence of infection and inflammation which may affect an individual's REE (Ferrie & Ward, 2007). Enrolment in a concurrent study by Paul Gittings (FSH Physiotherapist), 'Does exercise training improve muscle strength function after burn injury?' was recorded for consideration during analysis and was not considered an exclusion criterion.

2.3.2 Measured resting energy expenditure

Measured REE (mREE) was completed with the Ultima CPX (Medgraphics, USA) using a face tent to capture inspired and expired gas. The face tent was chosen as it is the recommended equipment for nutrition REE measurements for the Ultima CPX (MGC Diagnostics, 2012) and is disposable, thus meeting FSH infection control requirements. A bacterial filter (Bird Healthcare, Australia) was attached to meet the infection control requirements of FSH. According to the manufacturer's instructions, adjustments were made to the Ultima CPX settings to account for the resistance and dead space of the bacterial filter. Pre-study testing indicated that the bacterial filter did not affect the accuracy of measurements. *Figure 4* illustrates the setup of the collection system for the Ultima CPX.

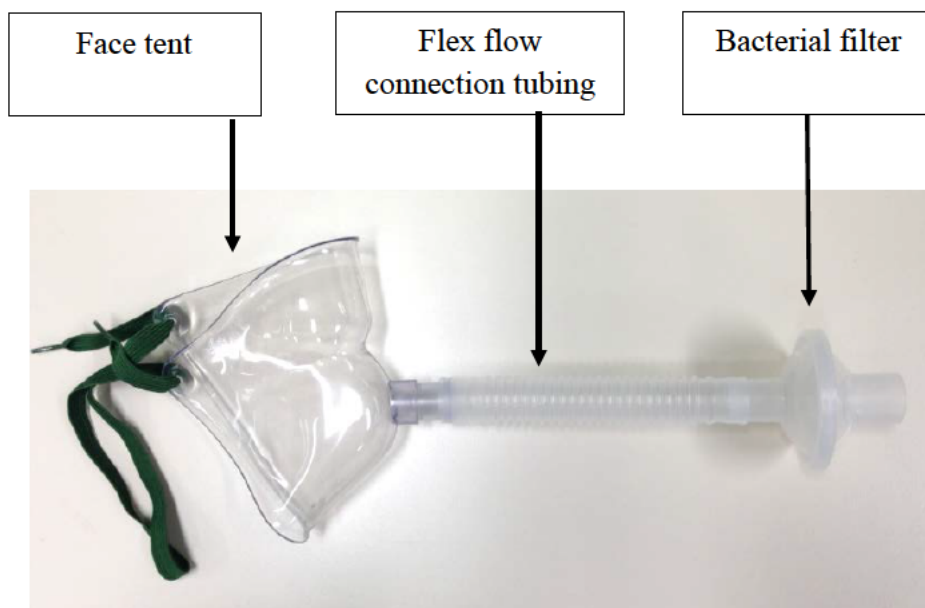


Figure 4. Ultima CPX face tent and bacterial filter set-up (photography by Janica Bell)

The Ultima CPX is an open-circuit system that measures oxygen consumption (VO_2) and carbon dioxide production (VCO_2) to calculate the REE using a modified Weir equation and the Respiratory Quotient (RQ); these are given in *Table 7*.

Table 7

The modified Weir equation for calculating resting energy expenditure and the Respiratory Quotient calculation (Moreira da Rocha et al., 2006; Shields et al., 2013)

$$\text{Weir equation REE (kcal)} = [(\text{VO}_2 \times 3.914) + (\text{VCO}_2 \times 1.106)] \times 1.44$$

$$\text{Respiratory Quotient} = \text{VCO}_2 / \text{VO}_2$$

Note. VO_2 = oxygen consumption (mL/min); VCO_2 = carbon dioxide production (mL/min)

The reproducibility and accuracy of the Ultima CPX has been demonstrated (Huszczuk, Whipp, & Wasserman, 1990; Porszasz, Barstow, & Wasserman, 1994) and the system has previously been used with hospitalised patients including those with burn injuries (Junejo et al., 2014; Peck et al., 2004; Pimenta et al., 2014; Wu, Huang, Xiao, Tang, & Cai, 2013). While originally designed for use with respiratory patients, additional software and collection systems are available for nutrition measurements. Indirect calorimetry measurements were recorded using the Breeze Suite Software (version 8.1, Medgraphics, USA). The Ultima CPX is registered with the Therapeutic Goods Administration (TGA) and accepted for use within Australia (*Appendix A*).

All REE measurements were obtained by the researcher between 0600 and 0700 hours, following administration of medications by nursing staff and prior to breakfast delivery, to obtain rested and fasted conditions. Medical procedures and wound dressings were performed after the indirect calorimetry measurement. The Ultima CPX was engaged for 30 minutes allowing the vacuum pump and gas analyser to warm up. The unit was then moved to the participant's room and calibration was completed according to the manufacturing protocol, described as follows. The PreVent pneumotach (Medgraphics, USA) was calibrated using a 3L calibration syringe to within 2% error. Room temperature, humidity and barometric pressure

were determined for calibration using the Vantage VUE wireless weather station (Davis, USA). Gas calibration was achieved using the automated system within the Ultima CPX unit and software. During calibration participants were instructed to rest on a bed in a supine position for 15 minutes without talking or sleeping. The face tent was then fitted to the participant with assistance from the researcher. A new face tent, flex flow tubing and bacterial filter was used for each measurement. Once the face tent was correctly fitted to the participant the fan speed controller was connected to the collection system using an elbow connection, as illustrated in *Figure 5*.

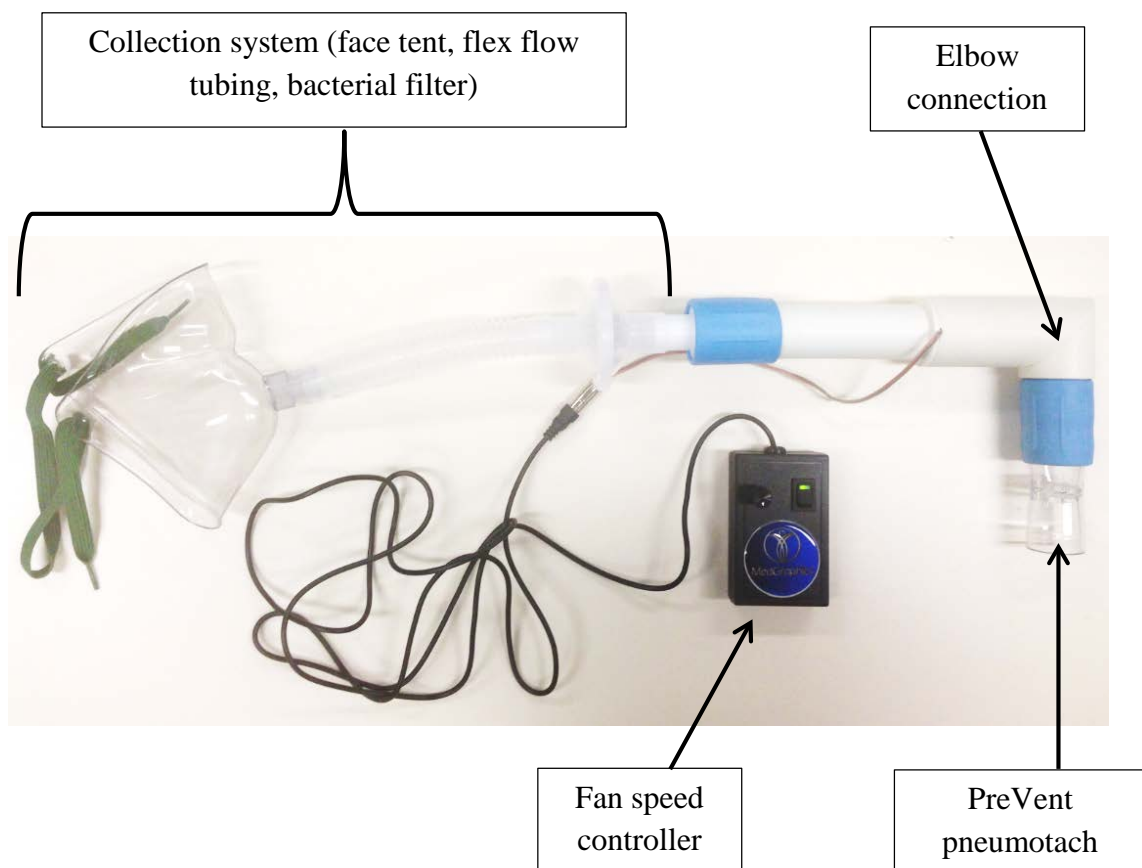


Figure 5. Ultima CPX fan speed controller set-up (photography by Janica Bell)

The fan speed was adjusted to maximise the carbon dioxide (CO₂) reading using the PWave display. Optimal CO₂ readings were considered a maximum value > 2% and a minimum value reaching 0% for approximately 1 second, as per manufacture's guidelines. Once achieved, the values were monitored for at least 2 minutes for stability prior to commencing the test. See **Figure 6** for an example PWave display.

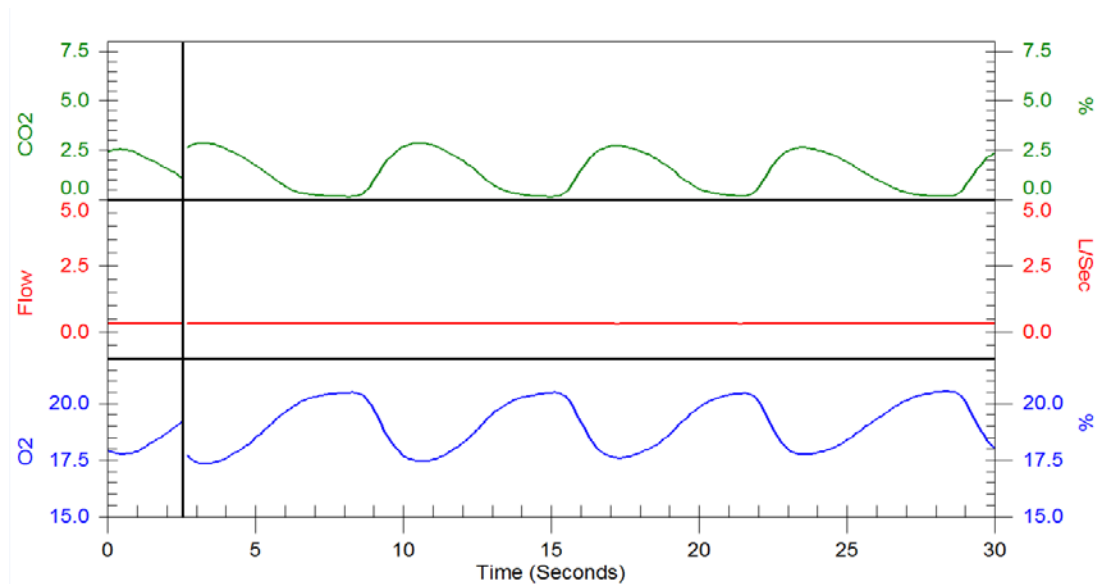


Figure 6. Ultima CPX PWave display illustrating the optimal variation of carbon dioxide (CO₂) readings for fan speed setup reaching 0% and exceeding 2% (reproduced from Breeze Suite Software output)

Quiet conditions were maintained during the measurement. Environmental conditions were monitored by the researcher throughout the measurement to ensure they did not deviate from the calibration conditions. The researcher monitored and noted any signs of agitation and movement by the participant during the measurement. Correct hand hygiene and the FSH personal protective equipment (PPE) protocol were followed at all times. At the end of each measurement the face tent, flex flow tubing and bacterial filter were discarded. At the end of

each test the surface of the Ultima CPX was cleaned using Oxivir® Tb wipes (Diversey, Netherlands).

The first five minutes of each indirect calorimetry test were discarded following best practice recommendations (Schlein & Coulter, 2013). Using a customised Microsoft Excel program (Microsoft, Washington, USA) developed by the researcher, the indirect calorimetry data was analysed in sixty second mean intervals to determine the presence of a steady state. A steady state period is a metabolic equilibrium that accurately reflects total REE over a 24 hour period (Holdy, 2004). This study employed a customised algorithm for the determination of a steady state. The algorithm was developed using literature and best practice recommendations and is given *Figure 7*.

The primary criterion for achievement of a steady state is a consecutive five minute period whereby the mean minute VO_2 and VCO_2 change by $\leq 10\%$ (Schlein & Coulter, 2013). If a steady state was not achieved using this criterion then a steady state, defined as the co-efficient of variation (CV) of VO_2 and VCO_2 changing by $\leq 5\%$ for 5 consecutive minutes, was applied (Schlein & Coulter, 2013). If a steady state was not achieved using either of these methods then a steady state, defined as the CV $\leq 10\%$ of the entire measurement, was applied (Schlein & Coulter, 2013). If none of the above methods achieved a steady state then the time period was reduced consecutively to 4 minutes, 3 minutes and then 2 minutes for both the VO_2 and VCO_2 changing by $\leq 10\%$ and the CV of VO_2 and VCO_2 changing by $\leq 5\%$. The final step in the algorithm, if no other criteria had achieved a steady state, was the analysis of the entire data set (excluding the first five minutes). The steady state period, defined according to the algorithm in *Figure 7* was used to determine the REE, VO_2 , VCO_2 and RQ for each indirect calorimetry measurement (Hart et al., 2002; Schlein & Coulter, 2013).

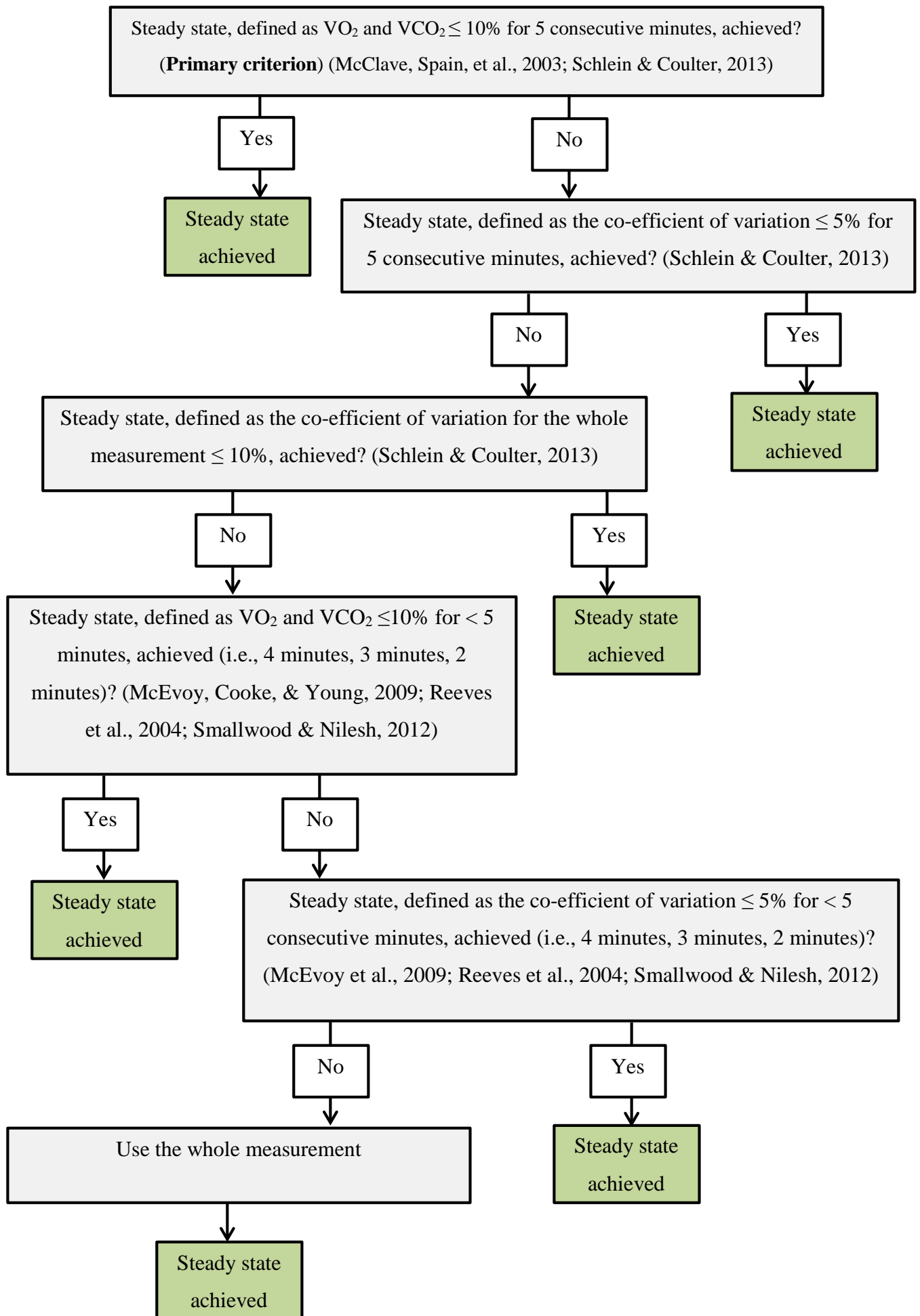


Figure 7. Algorithm for the determination of a steady state for indirect calorimetry measurements

2.3.3 Predicted resting energy expenditure

The predicted REE (pREE) was determined using the four most frequently cited equations in the literature, the Schofield, Harris-Benedict, Toronto and Ireton-Jones equations, and the energy-per-kilogram range of 100 to 125 kJ/kg of body weight/day. An injury factor was applied to the Schofield and Harris-Benedict equations. The equations, energy-per-kilogram ranges and injury factors are provided in **Table 8**. An adjustment to body weight was required for participants with a BMI is > 30 kg/m² (Edgar, 2014). The equation to calculate an adjusted body weight (ABW) is given in **Table 9**.

Table 9

Calculation to determine an adjusted body weight (Edgar, 2014)

$$ABW (kg) = [(current\ weight - IBW) \times 0.25] + IBW$$

Note. ABW = adjusted body weight; IBW = ideal body weight (kg) calculated as the weight equivalent to a BMI of 25 kg/m² for < 65 years of age or 27 kg/m² for > 65 years of age; current weight (kg)

The extent of hypermetabolism observed following a burn injury was quantified by calculating the difference between the predicted pre-burn REE, using both the Schofield and Harris-Benedict equations, and the initial mREE using indirect calorimetry. Results are expressed as a percentage increase from predicted pre-burn REE. Hypometabolism is defined as a measured REE, using indirect calorimetry, < 90% of the predicted REE, normometabolism is 90 to 110% and hypermetabolism is > 110% (Dickerson et al., 2002).

Table 8

Predictive models used to determine resting energy expenditure in the current study

Predictive model	Formula		Injury factors (IF)	
			TBSA	Factor
Harris-Benedict (Australian and New Zealand Burn Association, 2007)	Men (all ages)	$REE \text{ (kcal/day)} = [66.47 + (13.75 \times W) + (5.0 \times H) - (6.76 \times A)] \times IF$	< 10%	1.2
	Women (all ages)	$REE \text{ (kcal/day)} = [655.1 + (9.56 \times W) + (1.85 \times H) - (4.68 \times A)] \times IF$	11 – 20%	1.3
Schofield (Australian and New Zealand Burn Association, 2007)	Men 18 – 30 years	$REE \text{ (MJ/day)} = [(0.063 \times W) + 2.896] \times IF$	<10%	1.0 – 1.1 (for analysis, TBSA 0% = 1.0, TBSA 5% = 1.05, TBSA 10% = 1.1)
	Men 30 – 60 years	$REE \text{ (MJ /day)} = [(0.048 \times W) + 3.653] \times IF$		
	Men > 60 years	$REE \text{ (MJ /day)} = [(0.049 \times W) + 2.459] \times IF$		
	Women 18 – 30 years	$REE \text{ (MJ /day)} = [(0.062 \times W) + 2.036] \times IF$		
	Women 30 – 60 years	$REE \text{ (MJ /day)} = [(0.034 \times W) + 3.538] \times IF$		
	Women > 60 years	$REE \text{ (MJ /day)} = [(0.038 \times W) + 2.755] \times IF$	10 – 25%	1.1 – 1.3

Note. REE = resting energy expenditure; IF = injury factor; n/a = not applicable; W = weight (kg); H = height (cm); A = age (years); O = obesity defined as a body mass index > 27 kg/m² (1 = present; 0 = absent); %TBSA = % of total burn surface area; CI = calories received in the previous 24 hours; EBEE = estimated basal energy expenditure using the Harris-Benedict equation; T = average hourly body temperature for the previous 24 hours (°C); PBD = post burn days.

Table 8 (continued)

Predictive models used to determine resting energy expenditure in the current study

Predictive model	Formula	Injury factors (IF)	
		TBSA	Factor
Ireton-Jones (Ireton-Jones & Jones, 2002)	REE (kcal/day) for spontaneously breathing patients = $629 - (11 \times A) + (25 \times W) - (609 \times O)$	-	-
Toronto (Allard et al., 1990)	REE (kcal/day) = $-4343 + (10.5 \times \%TBSA) + (0.23 \times CI) + (0.84 \times EBEE) + (114 \times T) - (4.5 \times PBD)$	-	-
Energy-per-kilogram (Edgar, 2014)	Lower end of range 100 kJ/kg/day Upper end of range 125 kJ/kg/day	-	-

Note. REE = resting energy expenditure; IF = injury factor; n/a = not applicable; W = weight (kg); H = height (cm); A = age (years); O = obesity defined as a body mass index > 27 kg/m² (1 = present; 0 = absent); %TBSA = % of total burn surface area; CI = calories received in the previous 24 hours; EBEE = estimated basal energy expenditure using the Harris-Benedict equation; T = average hourly body temperature for the previous 24 hours (°C); PBD = post burn days.

2.3.4 Acceptability of indirect calorimetry measurements

Patient acceptability of the indirect calorimetry measurement was assessed using a written questionnaire (*Appendix B*). The questionnaire was developed by researchers in an unpublished study investigating the acceptability of indirect calorimetry measures with spinal patients at the Princess Alexandra Hospital (Brisbane, QLD). National and international experts in the use of indirect calorimetry measurements were sought by the Queensland researchers to develop the questionnaire. Permission was obtained to use the questionnaire in this study (A. Nevin, personal communication, July 7, 2014).

The questionnaire had 14 questions with responses that were rated using a Likert scale, yes or no categories, and one open ended response. The Likert scale provided a response from 1 to 5, with 1 indicating a strong agreement and 5 indicating a strong disagreement. The questionnaire took approximately 5 to 10 minutes to complete. Participants were asked to rate the time taken for the measurement, the timing of the measurement, the privacy provided during the measurement, and if they would be willing to repeat the test in the future or feel the test was appropriate for routine burn care. For the yes or no questions participants were asked to consider if they felt comfortable during the measurement, the acceptability of the room temperature, the ability to breathe normally, ability to remain still, if they experienced pain, and if they felt the urge to empty their bladder or bowel. For the open ended responses participants were asked to consider anything that would improve the measurement. The questionnaire was provided to participants by the researcher following the indirect calorimetry measurement. Either the researcher or the FSH burn unit dietitian returned later the same day or on a subsequent day to collect the completed questionnaires from participants.

2.3.5 Anthropometric measurements

Nutritional status was determined using hand grip strength (HGS) and the Patient Generated-Subjective Global Assessment (PG-SGA). HGS is a reliable and valid tool for acute burn injuries (Clifford, Hamer, Philips, Wood, & Edgar, 2013) which can be used to ascertain the muscle strength of an individual and thus identify their nutritional status (Norman, Stobäus, Gonzalez, Schulzke, & Pirlich, 2011). It is potentially useful as an early indicator of poor nutritional status and malnutrition (Flood, Chung, Parker, Kearns, & O'Sullivan, 2014). Hand grip strength was determined using a Jamar Hydraulic Hand Dynamometer (Sammons Preston Rolyan, USA) following the indirect calorimetry measurement.

Participants without a hand or arm injury completed the measurement. The participant was seated on a bed with their dominant arm flexed at a 90° angle and their wrist in a neutral position. The researcher then instructed the participant to complete a contraction for three seconds with the standard encouragement “squeeze as hard as you can, harder, harder, harder”. This was repeated three times with no less than 10 seconds and no more than 30 seconds between each measurement (Flood et al., 2014). Predictive equations, shown in **Table 10** were used to interpret hand grip strength measures with normal being considered a value $\geq 85\%$ of the predicted value (The National Isometric Muscle Strength (NIMS) Database Consortium, 1996). Participants with multiple hand grip strength measurements were analysed for change over time.

The PG-SGA is a tool used to determine the presence and severity of malnutrition and has been previously validated in oncology patients (Bauer, Capra, & Ferguson, 2002). The assessment is based on weight history, food intake, nutrition impact symptoms, restrictions to functioning and a physical examination. Patients are scored as either a “stage A” which is considered well-nourished, a “stage B” which is considered moderately malnourished or suspected malnutrition,

or a “stage C” which indicates severe malnutrition. A numeric value is also obtained which can be used to triage the patient and identify the severity, or risk of, malnutrition (Bauer et al., 2002). The PG-SGA was completed following the indirect calorimetry measurement by the researcher who is trained and experienced in the assessment tool. *Appendix C* provides the PG-SGA. Participants with multiple PG-SGA scores were analysed for change over time.

Table 10

Hand grip strength predictive equations (Flood et al, 2014)

$$\text{Left hand grip strength} = (A \times -0.16) + (G \times 16.68) + (\text{BMI} \times 0.29) + 26.6$$

$$\text{Right hand grip strength} = (A \times -0.18) + (G \times 16.9) + (\text{BMI} \times 0.23) + 31.33$$

Note. A = age (years); G = gender (male = 1 and female = 0); BMI = body mass index (kg/m²)

Body mass (kg) and height (cm) were obtained following the indirect calorimetry measurement. Electronic scales (Tanita, Australia) were used to determine body mass and values recorded to the nearest 0.1 kg. Height was determined using a stadiometer (Seca, Australia) to the nearest 0.1 cm. Participants were wearing light clothing and no shoes for measurements. Body mass index (kg/m²) (BMI) was calculated using Quetelet’s index, weight divided by square of height (Lee & Nieman, 2013), and classified as either underweight, healthy weight, overweight or obese, as shown in **Table 11**. Participants with multiple weight measurements were analysed for change over time.

Table 11

Body mass index classification for adults (World Health Organisation, 2000)

BMI (kg/m²)	Classification
< 18.5	Underweight
18.5 – 24.9	Healthy weight
24.9 – 29.9	Overweight
> 30	Obese

Note. BMI = body mass index

2.3.6 Dietary measurement

Dietary intake was determined using a multi-pass 24 hour food recall (Lee & Nieman, 2013) conducted by the researcher following the indirect calorimetry measurements. The 24 hour recall method was selected as it has a low respondent burden, is quick to administer and is designed to assess recent energy and nutrient intake (Barrett-Connor, 1991; Lee & Nieman, 2013). The gold standard in dietary assessment, the three-day weighed food recorded, was not used as it has a high subject burden (Lee & Nieman, 2013) and was considered inappropriate for acutely unwell hospitalised burn patients. The participant was asked to recall all food and beverages consumed in the previous 24 hours, starting with the first item after waking in the morning. The reported diet was recorded by the researcher. Information on percentage of meal consumed and brands were collected where relevant. The researcher probed for omitted or forgotten foods to improve the accuracy of the measurement (Lee & Nieman, 2013).

Foods served by the FSH catering department at breakfast, lunch and dinner were analysed using the FSH catering program Delegate (Delegate Technology GmbH, Austria). The FSH menu has previously been analysed using AUSNUT 2007 database (Foodworks Profession Edition version 7.0, Xyris Software, QLD) by FSH dietetic staff and this data was accessed by the researcher. Meals could be analysed as quarter fractions (0%, 25%, 50%, 75% or 100%) using the Delegate software. Foods consumed between main meals or those not provided by the hospital were analysed by the researcher using the AusFoods 2007 database (Foodworks Professional Edition version 7.0, Xyris Software, QLD). All foods were analysed for their energy (kJ/day) and protein (g/day) content. Energy intake was compared to REE, determined using indirect calorimetry or the Schofield equation, and total energy expenditure (TEE). TEE was estimated by applying an activity factor, as listed in **Table 12**, to the REE. Participant activity levels were described by the FSH burn unit physiotherapist based on therapy schedules and a corresponding physical activity factor was applied by the researcher. Thus the difference between energy consumed and energy expended, for both REE and TEE, was determined and reported as an absolute value (kJ) and relative difference (%).

Table 12

Physical activity factors for hospitalised patients (Ferrie & Ward, 2007)

Description of daily activity level	Physical activity factor^a
Sedated or almost always lying still	0.9 – 1.1
Bed rest (able to move self around the bed)	1.15 – 1.2
Occasionally mobilising on the ward	1.15 – 1.4
Mobilising frequently on the ward	1.4 – 1.5
Mobilising frequently on the ward with regular and intensive physiotherapy	1.5 – 1.6

^a REE is multiplied by the physical activity factor to produce an estimated TEE

Protein intake was compared to estimated protein requirements (g/kg of body weight/day) based on TBSA, as given in **Table 13**. The difference between protein intake and estimated protein requirements was determined and expressed as being within the protein range, above or below the range.

Table 13

Recommended protein intake ranges according to total body surface area (Edgar, 2014)

TBSA (%)	Protein (g/kg/day)
< 15%	1.0 – 1.5
15 – 30	1.5
31 – 49	1.5 – 2.0
> 50%	2.0 – 2.3

Protein intake was also expressed as a percentage of total energy consumed with the calculation given in **Table 14**.

Table 14

Calculation for the determination of protein intake as a percentage of total energy based on data from the 24 hour dietary recall

$$\text{Protein (\%)} = \frac{\text{protein (g)} \times 16^{\text{a}}}{\text{energy intake (kJ)}} \times 100$$

^a Atwater factor for protein (16 kJ/g)

2.4 Procedure

Patients admitted to the FSH Burn Unit were screened by the FSH Burn Unit dietitian in liaison with the ECU researcher. Patients meeting the inclusion criteria were approached by the FSH Burn Unit dietitian and provided with information about the study, both verbally and in writing using the “Study Flyer” (*Appendix D*). This process was mandated by FSH HREC. Patients who agreed to participate became the study cohort and informed written consent was obtained by the researcher using the “Patient Information and Consent Form” (*Appendix E*). Each participant was allocated a unique study identification code to maintain confidentiality and the researcher maintained a participant identification code document which was securely stored onsite at FSH, as per HREC approval.

The Ultima CPX was used to determine REE on two occasions for the first two participants and then once for the remainder of the participants. This change to study procedure occurred as majority of participants were discharged from hospital prior to the second measurement, making this measurement unfeasible. Indirect calorimetry occurred no more than 72 hours following any type of surgery. After each indirect calorimetry measurement the following data were collected or determined: weight; height; BMI; current medications; biochemical data; HGS; PG-SGA score; and 24 hour energy and protein intake. Height and weight were obtained by the researcher unless the participant was unable to ambulate, in which case the measurements were completed by the Burn Unit physiotherapist according to previously described protocol. The written questionnaire was administered to participants following the indirect calorimetry measurement. Demographics, past medical history and burn injury data for each participant were obtained from the medical notes. The researcher used the BIMS program to record each participant’s enrolment into the study as required by FSH HREC. The study procedure is illustrated in *Figure 8* and the study timeline is given in *Appendix F*.

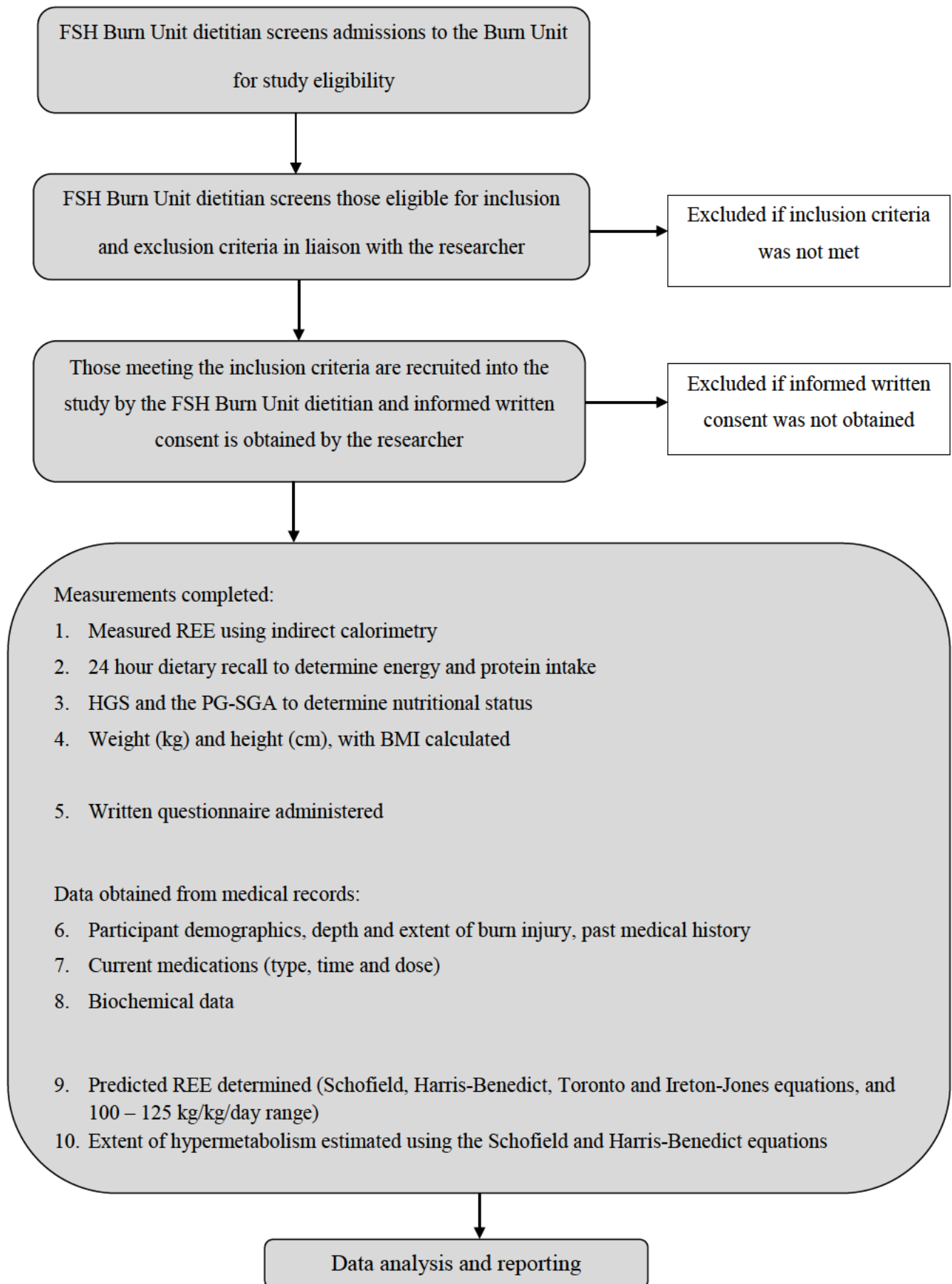


Figure 8. Study procedure

Note. FSH = Fiona Stanley Hospital; REE = resting energy expenditure; HGS = hand grip strength; PG-SGA = patient generated-subjective global assessment; BMI = body mass index

2.5 Statistical analysis

Statistical analyses were performed using IBM Statistical Package for the Social Sciences (SPSS) for Windows (version 21.0) (SPSS, Chicago, USA) or MS Excel (version 2010) (Microsoft, Washington, USA). Results are presented as the mean \pm standard deviation (range) with a p value ≤ 0.05 considered statistically significant. Difference was calculated between each steady state criterion and the primary criterion (see section 2.3.2); the difference between mREE and pREE for each predictive model (see section 2.3.3); and the difference between TEE and energy intake (see section 2.3.6), using the equation given in *Table 15*.

Table 15

Difference calculation

$$\text{Difference (\%)} = \frac{(\text{value 1} - \text{value 2})}{\text{value 1}} \times 100$$

2.5.1 Hypothesis 1

To test hypothesis 1, an independent t-test, with a test for unequal variances, was used to compare the mREE of the current study cohort (moderate burn injuries) to the published mREE of major burn injuries. Publications with major burn cohorts were included in the analysis if: all participants had a TBSA $\geq 15\%$; all participants were ≥ 18 years of age; the number of participants was reported; and the mean and standard deviation of the mREE were reported. The Cohen's test was used to determine the effect size between the mREE of moderate burn injuries and that of major burn injuries.

2.5.2 Hypothesis 2

Variation in mREE for moderate burn injuries over time was not analysed due to unforeseen modifications in the study protocol (see section 5.1.5). Instead, a case study examination of change in mREE over time was completed for a single participant who successfully completed two indirect calorimetry measurements on two different occasions. The mREE are reported in kJ/day and as the percentage difference between the two measurements and the predicted pre-burn REE determined using the Schofield and Harris-Benedict equations.

2.5.3 Hypothesis 3

To test hypothesis 3, scatterplots were generated to visually examine the association between mREE, and age, gender, BMI and TBSA. The influence of variables (age, gender, BMI, HGS, PG-SGA and burn injury) was not analysed using a statistical model due to the small number of participants (see section 3.1).

2.5.4 Hypothesis 4

To test hypothesis 4 the relative differences between the mREE using indirect calorimetry and pREE determined by each predictive method were obtained and reported in kJ/day and as the percentage difference between the two measures. Each predictive method was examined for accuracy, which was defined as $\pm 10\%$ of the mREE. An adjusted body weight was used in calculations for participants with a BMI ≥ 30 kg/m² (refer to section 2.3.3). Due to small participant numbers the pREE was not compared to the mREE using statistical models such as repeated measures General Linear Model (GLM).

2.5.5 Hypothesis 5

For analysis of patient responses in the questionnaire, single Likert scales questions were grouped as agreed, neutral or disagreed and reported as the absolute number of responses and as a percentage of the total number of responses. The 'agreed' group represents both strongly agreed and agreed, and the 'disagree' group represents both strongly disagree and disagree. The yes or no questions were reported as the number of responses for each category and as a percentage of the total. Written comments were reported verbatim.

Chapter: Results

3.1 Research population

A total of 27 patients admitted to the Fiona Stanley Hospital (FSH) Western Australian (WA) State Adult Burn Unit met the eligibility criteria of 5 to 15% total body surface area (TBSA) from the 11th March until the 30th of June and then < 15% TBSA from the 1st of July until the 31st of July 2015. Of the 27 patients, five declined to participate, eight had a facial burn injury and another three were deemed unable to provide informed consent; the remaining 11 participants enrolled in the study. Three participants were unable to complete the study due to scheduled surgery (n = 1), technical issues (n = 1) and the disbandment of one test due to an error in calibration (n = 1); the remaining eight participants completed the study and were included in the analysis. A flow diagram of study recruitment is given in *Figure 9*. Due to the smaller than anticipated sample size some of the planned statistical analysis could not be completed. Therefore, an analysis of individual burn patients and group trends is provided with the exception of hypothesis 1, which was statistically analysed as planned.

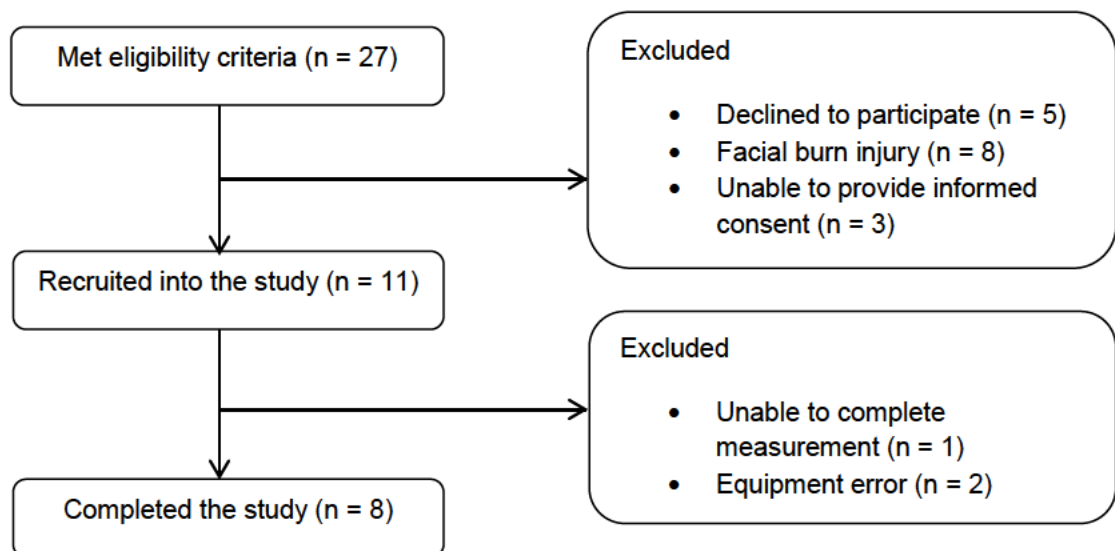


Figure 9. A flow diagram of study recruitment

There were three female and five male participants with a mean age of 48 ± 13 (29 – 62) years. The mean TBSA was $6.95 \pm 2.07\%$ with superficial partial burn injuries being the most common extent of injury, followed by superficial and deep partial. One participant experienced a partial burn injury, and no full thickness burn injuries occurred within the cohort. Flame was the most common burn agent (75%) and there was one scald (12.5%) and one hot oil (12.5%) injury. The mean time between the occurrence of burn injury and recruitment into the study was 6.11 ± 2.44 (3.42 – 11.50) days. Participant demographics and burn injury details are provided in **Table 16**. No participant was concurrently enrolled in the parallel study being undertaken at FSH titled: ‘Does exercise training improve muscle strength function after burn injury?’

Medications and potential effects on metabolism are summarised in **Table 17**. There were 23 different medications prescribed to the cohort, including analgesics (n = 7), antiemetics (n = 2), laxatives (n = 2), vitamin and mineral supplements (n = 5) and nicotine (n = 1). Analgesics and nicotine replacement therapy were the only group of drugs identified to affect REE (Moreira da Rocha et al., 2005; Schlein & Coulter, 2013; Wooley & Sax, 2003).

The biochemical values for albumin, total protein, white cell count (WCC), neutrophils and C-reactive protein (CRP) are given in **Table 18**. One participant did not have biochemical data available at the time of their indirect calorimetry measurement and CRP was unavailable for five participants. Albumin was below the reference range for four participants and in these participants CRP, where available, was elevated. The WCC and neutrophils were above the reference range in four participants.

Table 16

Participant characteristics (n = 8)

Participant number	Gender	Age (years)	Depth of burn injury					Extent of burn injury ^a (%)	Burn agent	PBD at time of recruitment (days)
			Superficial (%)	Superficial partial (%)	Partial (%)	Deep partial (%)	Full thickness (%)			
1	Female	60	1.75	4.00	-	-	-	5.75	Scald	3.42
2	Female	62	0.50	3.50	-	4.00	-	8.00	Flame	3.50
3	Male	61	-	7.70	-	-	-	7.70	Flame	6.58
4	Male	34	0.01	7.30	-	2.00	-	9.31	Flame	6.46
5	Male	29	-	2.50	2.50	-	-	5.00	Flame	6.21
6	Male	43	-	6.50	-	-	-	6.50	Flame	6.25
7	Male	40	1.50	4.60	-	3.50	-	9.60	Flame	5.25
8	Female	58	-	3.75	-	-	-	3.75	Hot oil	11.25
<i>Mean ± SD</i>		<i>48 ± 13</i>	<i>0.94 ± 0.82</i>	<i>4.98 ± 1.93</i>	<i>0.25</i>	<i>3.17 ± 1.04</i>	<i>-</i>	<i>6.95 ± 2.07</i>		<i>6.11 ± 2.44</i>
<i>Minimum</i>		<i>29</i>	<i>0.01</i>	<i>2.50</i>	<i>-</i>	<i>2.00</i>	<i>-</i>	<i>3.75</i>		<i>3.42</i>
<i>Maximum</i>		<i>62</i>	<i>1.75</i>	<i>7.70</i>	<i>-</i>	<i>4.00</i>	<i>-</i>	<i>9.60</i>		<i>11.50</i>

^a total body surface area (TBSA)

Note. PBD = post-burn days

Table 17

Medications prescribed to participants and their effects on resting energy expenditure

Medication	Purpose	Total frequency of prescription for the cohort	Effect on resting energy expenditure		
			Increase	Decrease	No effect
Paracetamol	Analgesic	8	-	✓	-
Pregabalin	Analgesic	8	-	✓	-
Oxycodone	Analgesic	6	-	✓	-
Tramadol	Analgesic	5	-	✓	-
Buprenorphine	Analgesic	1	-	✓	-
Tapentadol	Analgesic	1	-	✓	-
Celecoxib	Pain and inflammation	9	-	✓	-
Escitalopram	Antidepressant	2	-	-	✓
Lorazepam	Antianxiety	1	-	-	✓
Temazepam	Hypnotic	2	-	-	✓
Coloxyl and Senna	Laxative	6	-	-	✓
Lactulose	Laxative	5	-	-	✓
Ondansetron	Antiemetic	1	-	-	✓
Metoclopramide	Antiemetic	1	-	-	✓
Enoxaparin Sodium	Anticoagulant	2	-	-	✓
Amoxicillin	Antibiotic	1	-	-	✓
Phenergan	Antihistamine	1	-	-	✓
Magnesium sulphate	Correct hypomagnesemia	1	-	-	✓
Sodium phosphate	Correct hypophosphataemia	2	-	-	✓
Thiamine	Vitamin B1 supplementation	1	-	-	✓
Folic acid	Folic acid supplementation	1	-	-	✓
Vitamin B12	Vitamin B12 supplementation	1	-	-	✓
Nicotine patch	Nicotine replacement therapy	1	✓	-	-

Source: Moreira da Rocha et al. (2005); Wooley and Sax (2003); Fullmer et al. (2015); Schlein and Coulter (2013); Compher et al. (2006)

Table 18

Participant blood biochemical values

Participant number	Measurement number	Albumin (g/L)	Total protein (g/L)	White cell count (cells x 10 ⁹ per litre)	Neutrophils (cells x 10 ⁹ per litre)	C-Reactive protein (mg/l)
1	1	36	60	11.20 ^a	8.61 ^a	-
	2	-	-	-	-	-
2	1	40	67	10.50	6.55	-
	2	32 ^b	62	9.26	5.18	70 ^a
3	1	41	67	9.04	6.91	4
4	1	31 ^b	63	12.60 ^a	7.94 ^a	-
5	1	40	69	13.80 ^a	10.56 ^a	-
6	1	42	74	11.60 ^a	8.35 ^a	18 ^a
7	1	34 ^b	72	9.06	5.55	47 ^a
8	1	31 ^b	65	7.19	5.30	68 ^a
Reference range		35 - 50	60 - 80	4 – 11 x 10⁹	2 – 7.5 x 10⁹	< 5

^a biochemical data above the reference range

^b biochemical data below the reference range

3.2 Energy expenditure

3.2.1 Measured resting energy expenditure

A total of ten indirect calorimetry measurements were completed including two participants who completed the measurement on two different occasions. Steady state was determined using the algorithm provided in *Figure 7*. The measured resting energy expenditure (mREE) for each steady state criterion is given in **Table 19**. Two measurements (20%) achieved a steady state using the primary criterion and four measurements achieved a steady state using alternative criteria (40%). Four measurements (40%) were deemed to not achieve a steady state secondary to unforeseen error during the measurement, resulting in implausibly low resting energy expenditure (REE). The four tests were not considered accurate and were excluded from further analysis. In total, 60% (n= 6) of the measurements achieved a steady state and have undergone further analysis in this report. These measurements are in bold in **Table 19**.

Figure 10 shows a graphical representation of the continuous measurement of oxygen consumption (VO_2), carbon dioxide consumption (VCO_2), REE and respiratory quotient (RQ) over 20 to 30 minutes for three participants during the indirect calorimetry measurement. In graph a) the participant was relaxed and awake for the entire measurement and therefore achieved a steady state using the primary criterion between 9 and 18 minutes. In graph b) the participant oscillated between awake and asleep during the measurement and achieved a steady state using a 2 minute definition observed as the flattening of the lines between 15 and 17 minutes. In graph c) the participant experienced agitation and frequent movements throughout the test; a steady state was determined by averaging the entire measurement as a consecutive period of steady state, defined by all other criteria, was not identified.

Table 19

Achievement of the measured resting energy expenditure using the steady state criteria

Participant number	Measurement number	Steady state defined as VO ₂ and VCO ₂ < 10% ^a				Steady state defined as the CV < 5% ^a				Steady state defined as the CV < 10% for the entire measurement ^a	Average REE for the whole measurement ^a (kJ/day)
		(kJ/day)				(kJ/day)					
		5 minutes ^b	4 minutes	3 minutes	2 minutes	5 minutes	4 minutes	3 minutes	2 minutes		
1	1	-	-	-	-	-	-	-	-	-	5506
	2	-	-	-	-	-	-	-	-	-	6250
2	1	5448	5557	5576	5626	5472	5557	5576	5626	-	5519
	2	-	-	-	-	-	-	-	-	-	3245 ^c
3	1	-	-	-	-	-	-	-	5550	-	5632
4	1	-	-	-	6571	-	-	-	6571	-	6899
5	1	9639	9777	9817	9700	9639	9773	9817	9700	9380	9363
6	1	-	-	-	-	-	-	-	-	-	3272 ^c
7	1	-	-	-	-	-	-	-	-	-	4169 ^c
8	1	-	-	-	3764 ^c	-	-	3758 ^c	3764 ^c	-	3856 ^c

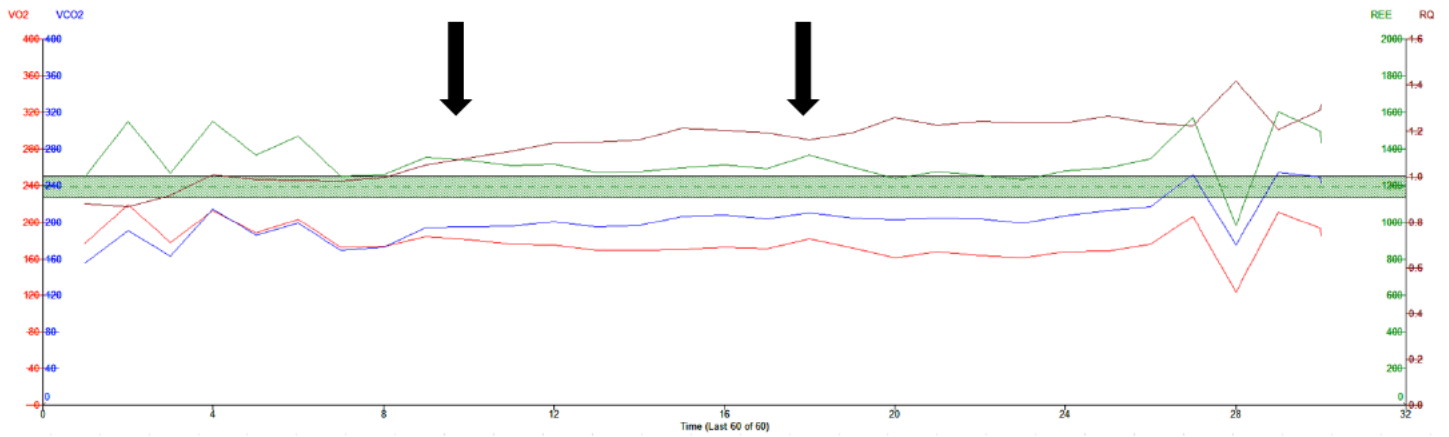
^a First five minutes of test excluded

^b Primary criterion

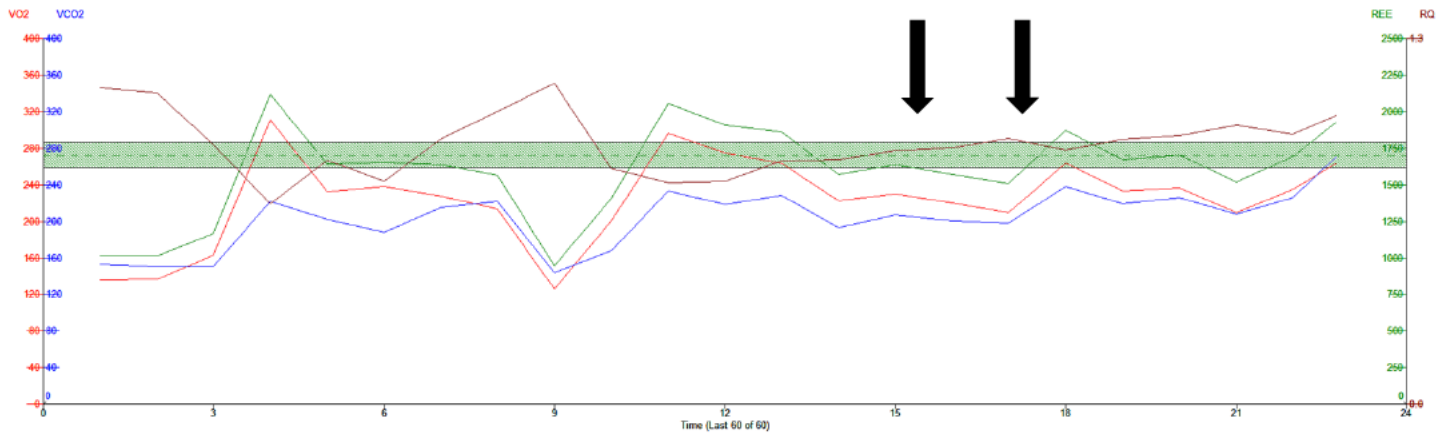
^c Unforeseen error in measurement resulting in implausibly low mREE

Note. Values in bold are taken as the most accurate steady state measurements (see algorithm in *Figure 7*) and are considered the measured resting energy expenditure for the participant; CV = co-efficient of variation; VO₂ = oxygen consumption (ml/min); VCO₂ = carbon dioxide production (ml/min)

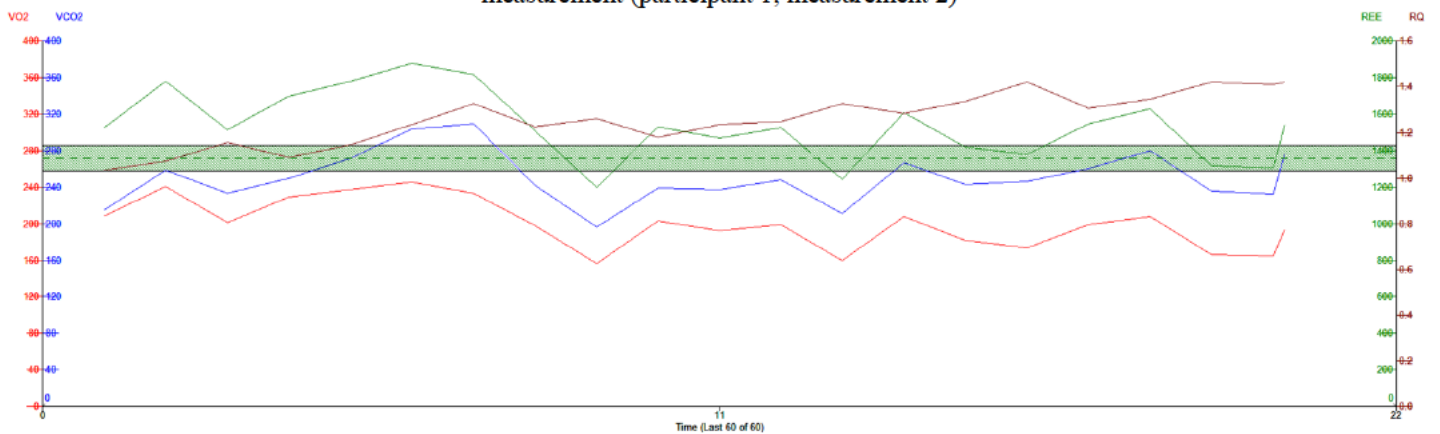
a) Rested and awake participant with minimal movement; steady state achieved using the primary criterion (participant 2, measurement 1)



b) Participant cycling between awake and sleep; steady state achieved using a 2 minute criterion (participant 4)



c) Agitated participant with frequent movement during the test; steady state achieved by averaging the whole measurement (participant 1, measurement 2)



Key

y axis: **Oxygen consumption (VO₂) (ml/min)** **Carbon dioxide production (VCO₂) (ml/min)** **Resting energy expenditure (REE) (kcal/day)** **Respiratory quotient (RQ)**

X axis: Time (minutes)

± 10% of the predicted REE using the Harris-Benedict equation Indicate period of steady state

Figure 10. Graphical representation of three indirect calorimetry resting energy expenditure measurements to demonstrated achievement of steady state (specified in Figure 7) reproduced from Breeze Suite software

Exploratory subset analysis was completed for participants 2 and 5 to investigate the variation between the methods of defining a steady state, as described in *Figure 7*. The primary criterion, i.e. a steady state defined as VO_2 and $\text{VCO}_2 \leq 10\%$ for 5 consecutive minutes, was compared to all other methods and the difference is reported in **Table 20**. The mean \pm SD (range) difference between the primary criterion and all other methods was $2.13 \pm 0.95\%$ (0.45 – 3.28%) for participant 2 and $0.25 \pm 1.82\%$ (-2.85 – 1.86%) for participant 5, corresponding to 116 kJ/day and 24 kJ/day difference, respectively. There was a trend towards a smaller percentage difference with increasing time to achieve steady state in participant 2 but not participant 5. The method with the lowest difference for both participant 2 and 5 was the steady state defined as 5 minutes with a co-efficient of variation $\leq 5\%$.

Table 21 provides a summary of the mREE outputs and environmental conditions for the eight participants. The mean mREE for the cohort was 6494 ± 1625 (5448 – 9639) kJ/day. The mean RQ was 1.08 ± 0.14 (0.91 – 1.31) which is greater than the recommended test validation range of 0.7 to 1.0 but within the physiological range of 0.7 to 1.3 (Compher et al., 2006; Schlein & Coulter, 2013). Of the six participants with RQ data, one had an RQ within the validation range (17%) and five had RQ values greater than the validation range (83%), three of which are within 6% of the range and two more than 15% above the range. The mean VO_2 and VCO_2 were 211 ± 55 (174 – 317) ml/min and 225 ± 52 (188 – 319) ml/min, respectively. The VCO_2 was above the physiological range in three participants which corresponded with the three highest RQ values. Environmental conditions including temperature, barometric pressure and humidity recorded at the time of calibration are given in **Table 21**. These conditions did not deviate from the recommended conditions for indirect calorimetry testing (Fullmer et al., 2015).

Table 20

Analysis of steady state criteria compared to the primary criterion for participants 2 and 5, as described in Figure 7

Method for determination of steady state	Participant 2		Participant 5		
	Value (kJ)	Difference ^b (%)	Value (kJ)	Difference ^b (%)	
Steady state defined as VO₂ and VCO₂ ≤ 10%	5 minutes^a	5448	-	9639	-
	4 minutes	5557	2.01	9777	1.44
	3 minutes	5576	2.36	9817	1.86
	2 minutes	5626	3.28	9700	0.63
Steady state defined as the co-efficient of variation ≤ 5%	5 minutes	5472	0.45	9639	0
	4 minutes	5557	2.01	9773	1.39
	3 minutes	5576	2.36	9817	1.86
	2 minutes	5626	3.28	9700	0.63
Steady state defined as the CV ≤ 10% for the whole measurement	n/a	n/a	9380	-2.69	
Average REE for the whole measurement	5519	1.31	9363	-2.85	
<i>Mean ± SD</i>	5551 ± 62	2.13 ± 0.95	9660 ± 166	0.25 ± 1.82	
<i>Minimum</i>	5448	0.45	9363	-2.85	
<i>Maximum</i>	5626	3.28	9817	1.86	

^a Primary criterion for the determination of steady state

^b Determined as the relative difference between the primary criterion and the alternative criteria

Note. CV = co-efficient of variation

Table 21

Summary of the measured resting energy expenditure outputs and environmental conditions

Participant number	Measurement number	mREE (kJ/day)	RQ	VO ₂		VCO ₂		Room temperature at calibration (°C)	Barometric pressure at calibration (mmHg)	Humidity at calibration (%)
				(mL/min)	(mL/min/kg ^c)	(mL/min)	(mL/min/kg ^c)			
1	1	5506	1.05 ^a	179	2.48	188	2.61	25	763.5	47
	2	6250	1.31 ^a	193	2.68	252	3.50 ^d	25	751.2	76
2	1	5448	1.15 ^a	174	3.04	200	3.50 ^d	23	762.6	46
	2	-	-	-	-	-	-	24	751.2	76
3	1	5550	1.06 ^a	181	2.44	190	4.33 ^d	22	760.1	46
4	1	6571	0.91 ^b	221	3.05	200	2.76	23	768.4	43
5	1	9639	1.01 ^a	317	2.95	319	2.97	23	767.5	47
6	1	-	-	-	-	-	-	23	766.1	47
7	1	-	-	-	-	-	-	22	761.0	56
8	1	-	-	-	-	-	-	22	755.0	68
<i>Mean ± SD</i>		<i>6494 ± 1625</i>	<i>1.08 ± 0.14</i>	<i>211 ± 55</i>	<i>2.77 ± 0.28</i>	<i>225 ± 52</i>	<i>3.28 ± 0.63</i>	<i>23 ± 1</i>	<i>760.7 ± 6.3</i>	<i>55 ± 13</i>
<i>Minimum</i>		<i>5448</i>	<i>0.91</i>	<i>174</i>	<i>2.44</i>	<i>188</i>	<i>2.61</i>	<i>22</i>	<i>751.2</i>	<i>43</i>
<i>Maximum</i>		<i>9639</i>	<i>1.31</i>	<i>317</i>	<i>3.05</i>	<i>319</i>	<i>4.33</i>	<i>25</i>	<i>768.4</i>	<i>76</i>

^a RQ greater than the specified validation range (0.7 – 1.0)

^b RQ within the validation range (Compher, Frankenfield, Keim, & Roth-Yousey, 2006; Reeves, Davies, Bauer, & Battistutta, 2004; Smallwood & Nilesh, 2012)

^c kg of actual body weight

^d VCO₂ greater than the physiological range (1.4 – 3.1 ml/min/kg) (Moreira da Rocha, Alves, Silva, Chiesa, & da Fonseca, 2006)

Note. RQ = respiratory quotient; mREE = measured resting energy expenditure; VO₂ = oxygen consumption; VCO₂ = carbon dioxide production

3.2.2 Resting energy expenditure of moderate versus major burn injuries

The mean mREE of the current study, with moderate burn injuries defined as < 15% TBSA, was compared to that of major burns, defined as \geq 15% TBSA, using data from published studies (hypothesis 1). Three studies were identified and met the criteria; the mean TBSA varied from 20 to 48% TBSA (Garrel & de Jonge, 1993; Shields et al., 2013; Wall-Alonso et al., 1999). The mREE for the three major burn cohorts was 35 to 62% greater than the mREE of the current moderate burn cohort (**Table 22**). The mean REE for the Garrel and de Jonge (1993) cohort was 50% greater than the mREE of the current study with moderate burn injuries ($p < 0.05$, effect size -3.33). The mean REE for the Shields et al. (2013) cohort was 62% greater than the mREE of the current study ($p < 0.001$, effect size -2.49). The mean REE for the Wall-Alonso et al. (1999) cohort was 35% greater than the mREE of the current study ($p < 0.05$, effect size -1.39).

Table 22

Comparison of measured resting energy expenditure for moderate burn injuries (< 15% TBSA) from the current study to major burn injuries (\geq 15% TBSA) from published studies

Study	Mean TBSA (%)	Participants (n)	Age (years)	Gender (F/M)	REE Mean \pm SD (kJ/day)	P value	Effect size
Current study	6.95 \pm 2.07	6	43 \pm 13	3F 5M	6494 \pm 1625	-	-
Garrel and de Jonge (1993)	40.00 \pm 16.00	19	33 \pm 15	8F 11M	9744 \pm 3110	0.023 ^a	-3.33
Shields et al. (2013)	48.00 \pm 21.00	39	46 \pm 19	NR	10550 \pm 3085	0.000475 ^a	-2.49
Wall-Alonso et al. (1999)	20.00 \pm 3.81	5	33 \pm 10	3 F 4M	8761 \pm 1348	0.036 ^a	- 1.39

^a mREE of the major burn cohort is significantly different from mREE for the moderate burn cohort in the current study (independent t-test)

Note. F = female; M = male; NR = not reported

3.2.3 Extent of hypermetabolism

The extent of hypermetabolism for the five participants with a mREE is summarised in **Table 23**. The mean difference between pre-burn REE using the Schofield equation (6485 kJ/day) and initial mREE (6543 kJ/day) was $0.77 \pm 9.96\%$ (58 ± 670 kJ/day). Three participants were normometabolic and two participants were hypermetabolic. The mean difference between pre-burn REE using the Harris-Benedict equation (6620 kJ/day) and initial mREE was $-1.32 \pm 11.63\%$ (-77 ± 805 kJ/day). One participant was hypometabolic, two were normometabolic and two were hypermetabolic.

Table 23

Change in resting energy expenditure from pre-burn injury to post-burn injury

Participant number	Measured post-burn resting energy expenditure ^c		Pre-burn resting energy expenditure			
	REE (kJ/day)	PBD (days)	Schofield equation		Harris-Benedict equation	
			REE (kJ/day)	% ^a	REE (kJ/day)	% ^a
1	5506	3	5495	0.20	5718	-3.71
2	5448	3	4925	10.62	4945	10.17
3	5550	6	6080	-8.72	6541	-15.15
4	6571	6	7208	-8.84	7219	-8.98
5	9639	6	8717	10.58	8678	11.07
<i>Mean ± SD</i>	6543 ± 1792	5 ± 2	6485 ± 1507	0.77 ± 9.96	6620 ± 1433	-1.32 ± 11.63
<i>Minimum</i>	5448	3	4925	-8.84	4945	-15.15
<i>Maximum</i>	9639	6	8717	10.62	8678	11.07

^a Difference between first mREE and pre-burn REE

^b 13.59% (744 kJ/day) higher than the mREE on post-burn day 3

^c Using indirect calorimetry

Note. REE = resting energy expenditure' PBD = post-burn days

A case analysis of change in mREE over time was conducted for participant one who completed two indirect calorimetry measurements on two different occasions (hypothesis 2). The REE measured by indirect calorimetry (5506 kJ/day) on post-burn day (PBD) 3 was within $\pm 5\%$ of REE predicted by the Harris-Benedict (5718 kJ/day) and the Schofield equations (5495 kJ/day), and was 13.5% higher on PBD 15 (6250 kJ/day), by 744 kJ/day.

3.2.4 Influences on energy expenditure in burn injuries

The associations by gender between mREE and age, body mass index (BMI) and TBSA for the six participants with a mREE are shown in *Figure 11* (hypothesis 3). REE in participants < 40 years (both male) was higher than in participants aged > 40 years (2 female, 1 male); no trends in gender were apparent. BMI ranged from 22.6 to 30.7 kg/m²; the participant with the highest BMI, in the obese category (male), also had the highest mREE. No trends were observed for participants with a BMI < 27 kg/m² (2 male, 3 female). The extent of burn injury ranged from 5.00 to 9.60% for participants; no trend was apparent in the data. Participant 5 with the highest mREE had the lowest TBSA; this participant was also the youngest and had the highest BMI.

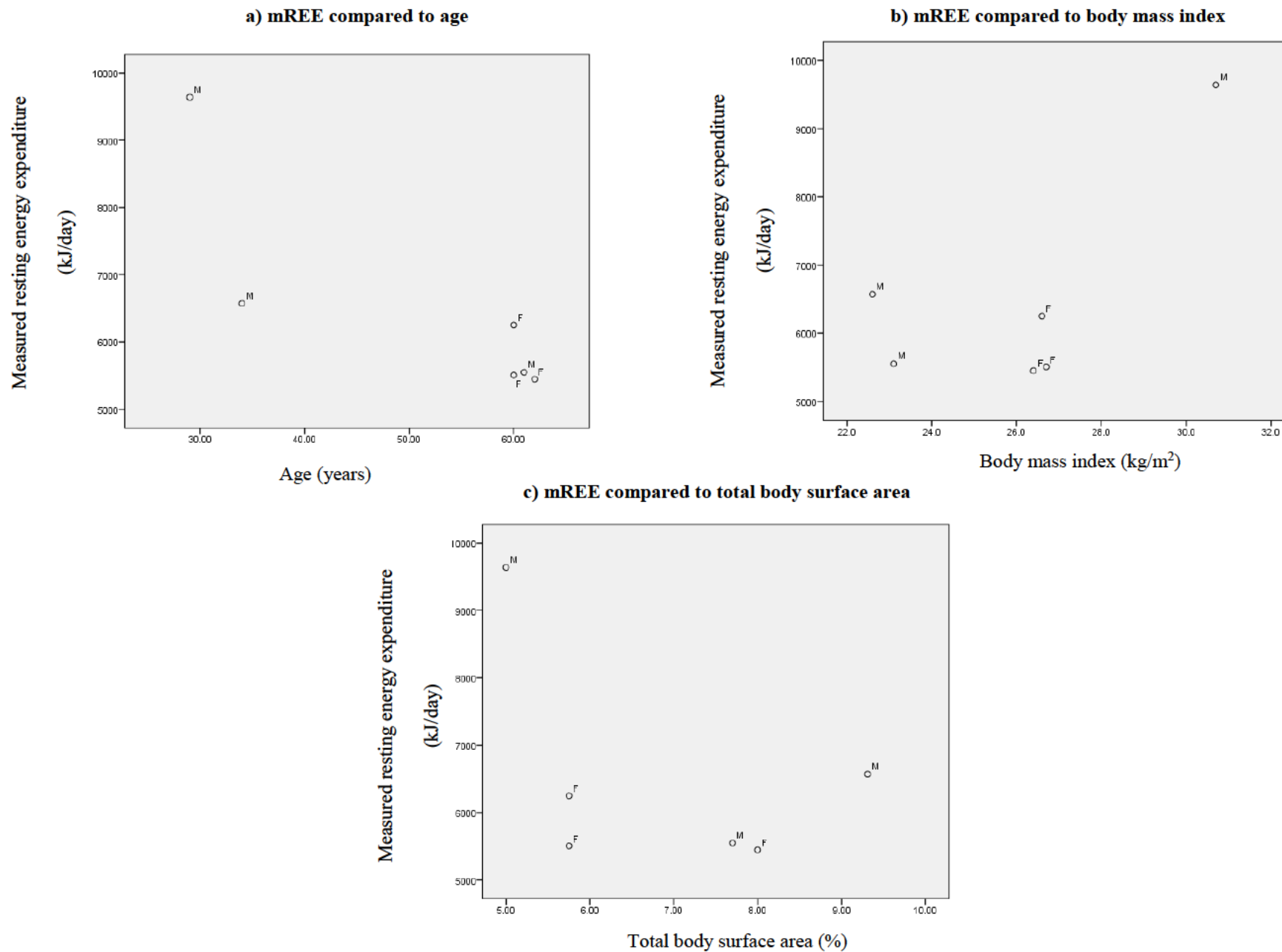


Figure 11. Association between measured resting energy expenditure for age (a), body mass index (b) and total body surface area (c) for six participants

Note. M = male; F = female; mREE = measured resting energy expenditure

3.2.5 Measured versus predicted resting energy expenditure

The relative difference between the predicted resting energy expenditure (pREE) and the mREE for the six participants is described in *Figure 12* and **Table 24** (hypothesis 4). The Schofield equation and the Toronto equation are accurate to within $\pm 10\%$ of the mREE, with a mean difference of 5.21% and 8.89%, respectively. Accuracy to within $\pm 10\%$ of the mREE was observed for four participants for the Schofield equation and three participants for the Toronto equation. The remaining predictive methods had a difference greater than $\pm 10\%$ of the mREE. The upper end of the energy-per-kilogram range had the highest difference at 43.78% with no participants having a pREE within $\pm 10\%$ of the mREE. This was followed by the Harris-Benedict equation with a difference of 32.14% with three participants having a pREE within $\pm 10\%$ of the mREE, the Ireton-Jones equation at 18.80% which had one participant within $\pm 10\%$ of the mREE, and the lower end of the range equation at 15.03% with two participants having a pREE within $\pm 10\%$ of the mREE. The lowest difference between the mREE and all predictive methods was observed in participant 5 at 0.21%, as illustrated in *Figure 12*. This was followed by participant 2 (test 1) with a mean difference of 10.13%, participant 1 (test 2) with 12.39%, participant 1 (test 1) with 27.80%, participant 4 with 29.81% and the largest difference was observed in participant 3 at 43.51%.

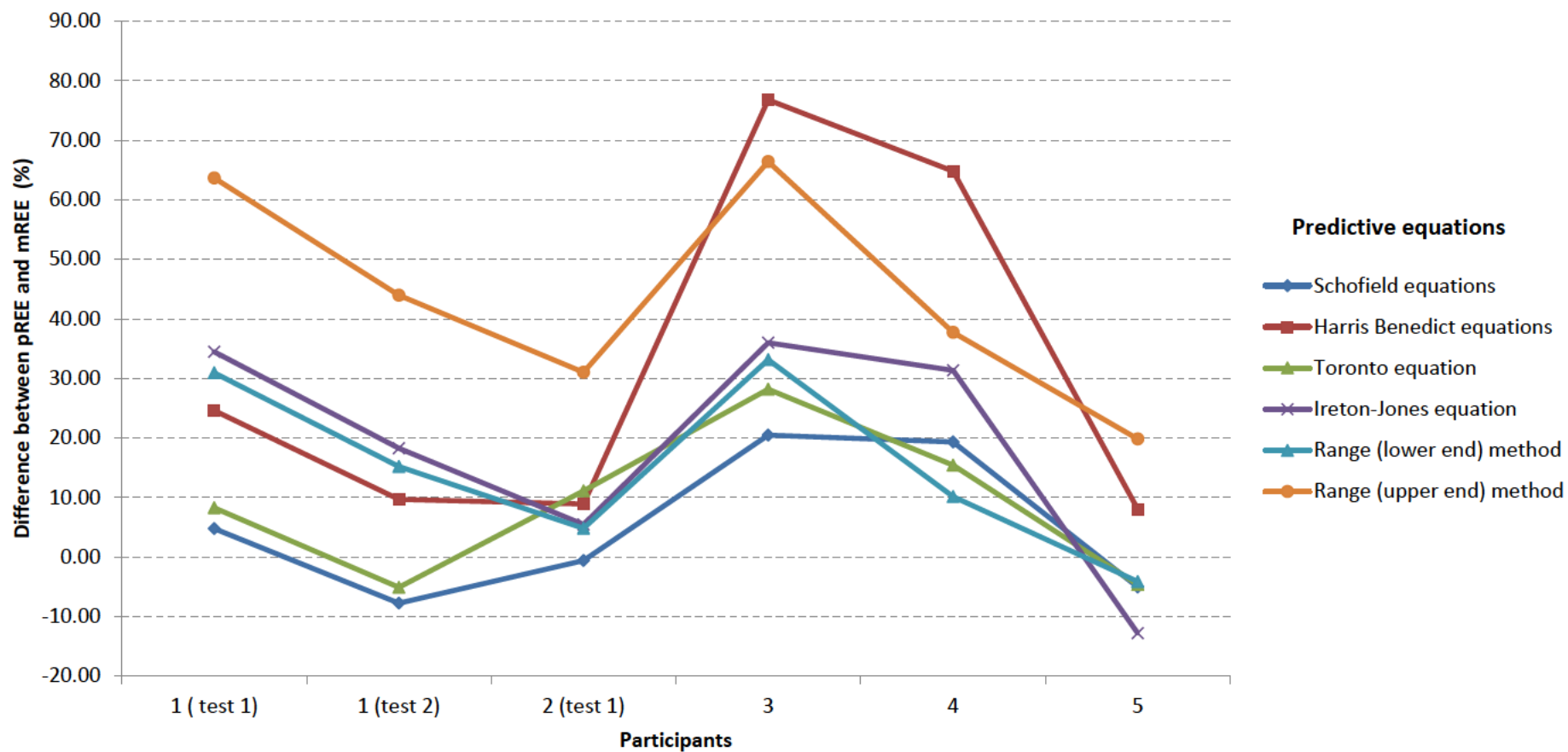


Figure 12. Difference between resting energy expenditure using predictive methods and measured resting energy expenditure using indirect calorimetry for six participants

Note. mREE = measured resting energy expenditure; pREE = predicted resting energy expenditure

Table 24

Evaluation of predictive equations compared to the measured resting energy expenditure using indirect calorimetry

Participant number	Measurement number	mREE	Schofield		Harris-Benedict		Toronto		Ireton-Jones		Range			
			(kJ/day)		(kJ/day)		(kJ/day)		(kJ/day)		Lower end		Upper end	
			Value	Diff. ^a	Value	Diff. ^a	Value	Diff. ^a	Value	Diff. ^a	Value	Diff. ^a	Value	Diff. ^a
			(kJ/day)	(%)	(kJ/day)	(%)	(kJ/day)	(%)	(kJ/day)	(%)	(kJ/day)	(%)	(kJ/day)	(%)
1	1	5506	5770	4.79	6861	24.62	5963	8.29	7405	34.49	7210	30.95	9013	63.68
	2	6250	5766	-7.76	6857	9.70	5932	-5.10	7394	18.30	7200	15.19	9000	43.99
2	1	5448	5417	-0.56	5934	8.92	6055	11.14	5745	5.46	5710	4.81	7138	31.02
	2	-	5405	-	5919	-	6637	-	5714	-	5680	-	7100	-
3	1	5550	6688	20.51	9811	76.77	7115	28.20	7547	35.98	7390	33.15	9238	66.44
4	1	6571	7841	19.33	10 829	64.80	7587	15.46	8632	31.36	7240	10.18	9050	37.73
5 ^b	1	9639	9153	-5.04	10 413	8.04	9193	-4.62	8406	-12.79	9240	-4.13	11 550	19.83
6	1	-	7217	-	7641	-	n/a [^]	-	7664	-	6710	-	8388	-
7	1	-	8057	-	8667	-	9117	-	8784	-	7650	-	9563	-
8	1	-	6076	-	6375	-	6525	-	6285	-	6050	-	7563	-
<i>Mean</i>		<i>6494 ± 1625</i>	<i>6739 ± 1285</i>	<i>5.21 ± 12.16</i>	<i>7931 ± 1870</i>	<i>32.14 ± 30.79</i>	<i>7125 ± 1274</i>	<i>8.89 ± 12.64</i>	<i>7358 ± 1123</i>	<i>18.80 ± 19.36</i>	<i>7008 ± 1061</i>	<i>15.03 ± 14.68</i>	<i>8760 ± 1326</i>	<i>43.78 ± 18.35</i>
<i>Minimum</i>		<i>5448</i>	<i>5405</i>	<i>-7.76</i>	<i>5919</i>	<i>8.04</i>	<i>5932</i>	<i>-5.10</i>	<i>5714</i>	<i>-12.79</i>	<i>5680</i>	<i>-4.13</i>	<i>7100</i>	<i>19.83</i>
<i>Maximum</i>		<i>9639</i>	<i>9153</i>	<i>20.51</i>	<i>10 829</i>	<i>76.77</i>	<i>9193</i>	<i>28.20</i>	<i>8784</i>	<i>35.98</i>	<i>9240</i>	<i>33.15</i>	<i>11 550</i>	<i>66.44</i>

^a Relative difference (%) between mREE by indirect calorimetry and calculated from the predictive method

^b adjusted body weight used to calculate the pREE

n/a[^] = inaccurate 24 hour recall therefore, the Toronto equation could not be completed

Note. mREE = measured resting energy expenditure

Comparison between use of an adjusted body weight (ABW) and actual body weight for the calculation of pREE for participant 5 is shown in **Table 25**. This participant has been examined as a case study to investigate the difference between using an ABW (92.4 kg) and actual body weight (107.35 kg) for the calculation of pREE as their BMI was ≥ 30 kg/m². The pREE using actual body weight was larger for all equations. The mean difference between the actual body weight and the ABW was $11.59 \pm 3.35\%$ (7.27 – 15.67%) with the Ireton-Jones equation observed to have the largest difference (15.67%) and the Toronto equation the smallest (7.27%). Estimates of REE based on ABW were used for further analysis (Edgar, 2014).

Table 25

Comparison of adjusted body weight and actual weight for the calculation of predicted resting energy expenditure in participant 5

Predictive equation		Actual body weight (kJ/day)	Adjusted body weight ^a (kJ/day)	Difference ^b (%)
Schofield		10 142	9153	9.75
Harris-Benedict		11 444	10 413	9.01
Toronto		9914	9193	7.27
Ireton-Jones		9968	8406	15.67
Range	Lower end	10 735	9240	13.92
	Upper end	13 419	11 550	13.92
<i>Mean ± SD</i>		<i>10 937 ± 1347</i>	<i>9659 ± 1128</i>	<i>11.59 ± 3.35</i>
<i>Minimum</i>		<i>9914</i>	<i>8406</i>	<i>7.27</i>
<i>Maximum</i>		<i>13 419</i>	<i>11 550</i>	<i>15.67</i>

^a Refer to section 2.3.3 for the adjusted body weight calculation

^b Relative difference (%) between the predicted resting energy expenditure calculated using an ABW and actual body weight

Five out of eight participants completed the entire questionnaire and one participant partially completed the survey (hypothesis 5). A summary of the questionnaire results is provided in **Table 26** and the qualitative statements given by participants are recorded in **Table 27**. There was 100% agreement with statements relating to the acceptable time taken to conduct the test and the time of the morning at which the testing occurred. All participants indicated that they experienced adequate privacy during the measurement and that they would be willing to repeat the measurement. Two participants indicated a neutrality regarding the measurement being acceptable for routine burn care with one participant suggesting "...research could be done on a few people to get a range for weight/ height etc then go off that...". All participants indicated that they felt comfortable during the measurement, the room temperature was acceptable, they could remain still and relaxed during the test and that they could breathe normally. Two participants noted that the face mask could be improved for a better and more comfortable fit (**Table 27**). No participants reported that they had the urge to empty their bladder or bowels during the procedure.

Table 26

Summary of the participant questionnaire

Question		Agreed	Neutral	Disagreed
1	The amount of time taken to complete the metabolic testing was acceptable	6 (100%)	0 (0%)	0 (0%)
2	The time of the morning the metabolic testing was undertaken was convenient to me	6 (100%)	0 (0%)	0 (0%)
3	I felt there was adequate privacy where the metabolic testing was undertaken	5 (100%)	0 (0%)	0 (0%)
4	I would be willing to have the metabolic testing procedure repeated in the future	5 (100%)	0 (0%)	0 (0%)
5	I feel it would be acceptable for patients with a burn injury to have metabolic testing measurements performed as part of their routine care	3 (60%)	2 (40%)	0 (0%)

Question		Yes	No
The following statements relate to your experience during the metabolic testing procedure:			
6	I felt comfortable during the procedure	6 (100%)	0 (0%)
7	The room temperature was acceptable	6 (100%)	0 (0%)
8	I was able to breathe normally with the face mask	6 (100%)	0 (0%)
9	I was able to remain still during the procedure	6 (100%)	0 (0%)
10	I was able to relax during the procedure	6 (100%)	0 (0%)
11	I felt pain during the procedure	0 (0%)	6 (100%)
12	I felt the urge to empty my bladder during the procedure	0 (0%)	6 (100%)
13	I felt the urge to open my bowels during the procedure	0 (0%)	6 (100%)

Note. Agreed represents “strongly agreed” and “agreed”, disagree represents “strongly disagree” and “disagree”

Table 27

Participant qualitative statements recorded on the questionnaire

Comment recorded
“it was an ok experience”
“perhaps the mask could be made more comfortable by using a wider headband”
“better fitting face mask, for beards”
“#5, I circled neutral because research could be done on a few people to get a range for weight/ height etc then go off that, save everybodys time ☺”
“No fine and easy, possible combination of other short researches such as “DNA silva (sic) test” etc. they might be run from different areas but these could be co-ordinated and less intrusive. If patients say no to one, then I’m sure they will so no to most and vise (sic) versa”

3.3 Nutritional status

The anthropometric and nutritional status data for participants is given in **Table 28**. Two participants, number 1 and 2, underwent measurements on two occasions; the change over time for these participants is reported. The mean weight for the cohort at the first measurement was 73.4 ± 15.3 (57.1 – 107.4) kg and the mean height was 170.6 ± 12.4 (147.1 – 187.0) cm. The mean BMI was 25.1 ± 2.9 (21.7 – 30.7) kg/m² with five participants within the healthy BMI category, two participants in the overweight category and one participant in the obese category. For participants 1 and 2, there was < 1% change in weight and BMI between the first and second measurement.

Results of nutritional status assessed using hand grip strength (HGS) and the Patient Generated-Subjective Global Assessment (PG-SGA) are provided in **Table 29**. HGS was completed by five participants and could not be completed for three participants secondary to burn injuries on their hands. In all instances the HGS score was within the healthy range. One participant

had their HGS completed on two separate occasions, 12 days apart, with < 1% difference between the first and second measurement.

The PG-SGA was completed by all participants. The mean score for the first measurement was 6 ± 2.62 (2 - 9). Four participants were classified as “requires intervention by dietitian, in conjunction with nurse or physician as indicated by symptoms survey”. Two participants were classified as “patient and family education by dietitian, nurse, or other clinician with pharmacologic intervention as indicated by symptoms survey and laboratory values as appropriate” and two participants classified as “...critical need for improved symptom management and/ or nutrition intervention options”. The most commonly reported symptoms were pain (n = 9); nausea (n = 5); constipation (n = 5), vomiting (n = 3); early satiety (n = 3); and a dry mouth (n = 1). In all instances participants were globally classified as “A - well nourished”. For the physical examination nine participants were classified as having no deficit in muscle or subcutaneous adipose stores and one was assessed as having a mild deficit. For the two participants who completed the PG-SGA on two separate occasions the scores changed by -44% and 20%, respectively, with no change in the global rating.

3.4 Dietary intake

The 24 hour recall was completed in nine participants with one participant unable to recall their intake. Energy and protein intake in comparison to requirements is given in **Table 29**. The mean energy intake in the 24 hours prior to the indirect calorimetry measurement was 9703 ± 2562 kJ (6496 – 14131 kJ) and mean protein intake was 91 ± 26 g (58 – 139 g).

Energy intake compared to REE, either measured or predicted, showed a mean excess of 2898 ± 2071 kJ/day (463 – 5848 kJ/day). Total energy expenditure (TEE) was determined by applying an activity factor of 50% to the REE. This activity factor was selected as the

participants completed a 30 minutes daily walking session and five times per week had a 30 minute aerobic and anaerobic gym session with a physiotherapist (P. Gittings, personal communication, August 10, 2015). The mean TEE was 9858 ± 207 kJ/day (8172 – 14459 kJ/day). The mean energy difference between intake and TEE was -47 ± 4378 kJ/day (- 4356 – 2530 kJ/day) or a mean difference of 2 ± 28 % (-30 – 54%).

Protein requirements were estimated using the range of 1.0 to 1.5 g/kg of body weight/day and are presented as the lower (1.0 g/kg/day) and the upper end of the range (1.5 g/kg/day) (Edgar, 2014). The mean daily estimated protein requirements were from 72 ± 14 g/day (57 – 107 g/day) to 107 ± 22 g/day (85 – 161 g/day). The estimated protein intake of four participants was within the lower and upper bounds of the estimated protein range, two participants had an estimated protein intake less than the range and three participants had an estimated protein intake above the range, with one participant exceeding by 1 gram. The contribution of protein to the total energy intake was 15 ± 6 % (9 – 27%). The recommended protein contribution range is 15 to 25%; five participants were within this range, three were below and one was above of the range.

Table 28

Nutritional status of participants

Participant number	Height (cm)	1 st measurement					2 nd measurement					Change			
		Weight (cm)	BMI (kg/m ²)	HGS (kg)	PG-SGA		Weight (cm)	BMI ^a (kg/m ²)	HGS (kg)	PG-SGA		Weight (%)	BMI ^a (%)	HGS (%)	PG-SGA score (%)
					Score	Category				Score	Category				
1	164.5	72.1	26.7 ^a	26.66 ^d	9	A	72.0	26.60 ^a	26.65 ^d	5	A	< 1	< 1	< 1	- 44
2	147.1	57.1	26.4 ^a	-	5	A	56.8	26.20 ^a	-	6	A	< 1	< 1	-	+ 20
3	178.9	73.9	23.1 ^b	-	6	A	-	-	-	-	-	-	-	-	-
4	179.0	72.4	22.6 ^b	-	9	A	-	-	-	-	-	-	-	-	-
5	187.0	107.4	30.7 ^c	50.07 ^d	8	A	-	-	-	-	-	-	-	-	-
6	165.0	67.1	24.6 ^b	46.15 ^d	6	A	-	-	-	-	-	-	-	-	-
7	176.0	76.5	24.7 ^b	46.71 ^d	2	A	-	-	-	-	-	-	-	-	-
8	167.0	60.5	21.7 ^b	25.88 ^d	3	A	-	-	-	-	-	-	-	-	-
<i>Mean ± SD</i>	<i>170.6 ± 12.4</i>	<i>73.4 ± 15.3</i>	<i>25.1 ± 2.9</i>	<i>39.09 ± 11.81</i>	<i>6 ± 2.62</i>		<i>64.6 ± 10.8</i>	<i>26.40 ± 0.28</i>		<i>5.50 ± 0.71</i>					<i>- 12 ± 46</i>
<i>Minimum</i>	<i>147.1</i>	<i>57.1</i>	<i>21.7</i>	<i>25.88</i>	<i>2</i>		<i>56.8</i>	<i>26.20</i>		<i>5.00</i>					<i>-44</i>
<i>Maximum</i>	<i>187.0</i>	<i>107.4</i>	<i>30.7</i>	<i>50.07</i>	<i>9</i>		<i>72.0</i>	<i>26.60</i>		<i>6.00</i>					<i>+ 20</i>

^a BMI classification of overweight^b BMI classification of healthy^c BMI classification of obese^d HGS within the healthy range

Note. PG-SGA (Patient Generated-Subjective Global Assessment) category A = well nourished; BMI = body mass index; HGS = hand grip strength

Table 29

Participant energy and protein intake compared to requirements

Participant number	Measurement	Energy intake ^a (kJ)	Measured or estimated REE (kJ)	Difference between energy intake and REE (kJ)	TEE ^b (kJ)	Energy difference of TEE and intake		Protein intake (grams)	Estimated protein requirements ^c (g/kg of body weight/day)		Within the protein range	Protein contribution of energy ^d (%)
						kJ	% ^g		Lower end of range	Upper end of range		
1	1	6496	5506 ^e	990	8259	-1763	-21	87	72	108	Yes	21
	2	7344	6250 ^e	1094	9375	-2031	-22	68	72	108	No (below)	15
2	1	9297	5448 ^e	3849	8172	1125	14	91	57	86	No (above)	16
	2	12 485	5405 ^f	7080	8108	4378	54	86	57	85	No (above)	11 ^h
3	1	8387	5550 ^e	2837	8325	62	1	83	74	111	Yes	11 ^h
4	1	7643	6571 ^e	1072	9856	-2214	-22	79	72	109	Yes	15
5	1	10 102	9639 ^e	463	14 459	-4357	-30	127	107	161	Yes	27
6	1	-	7217 ^f	-	10 826	-	-	-	67	101	-	-
7	1	14 131	8057 ^f	6074	12 086	2046	17	139	77	115	No (above)	16
8	1	11 443	6076 ^f	4918	9113	2331	26	58	60.	91	No (below)	9 ^h
<i>Mean ± SD</i>		<i>9703 ± 2562</i>	<i>6572 ± 1382</i>	<i>3203 ± 2498</i>	<i>9858 ± 2073</i>	<i>-47 ± 2764</i>	<i>-2 ± 28</i>	<i>91 ± 26</i>	<i>72 ± 14</i>	<i>107 ± 22</i>		<i>15 ± 6</i>
<i>Minimum</i>		<i>6496</i>	<i>5405</i>	<i>463</i>	<i>8172</i>	<i>-4356</i>	<i>-30</i>	<i>58</i>	<i>57</i>	<i>85</i>		<i>9</i>
<i>Maximum</i>		<i>14131</i>	<i>9639</i>	<i>7080</i>	<i>14459</i>	<i>4378</i>	<i>54</i>	<i>139</i>	<i>107</i>	<i>161</i>		<i>27</i>

^a Determined using a 24 hour recall

^b TEE calculated by multiplying the REE by an activity factor of 50%

^c Protein range of 1 – 1.5 g/kg/day

^d Calculated as a percentage of total energy intake

^e REE determined using indirect calorimetry

^f Calculated using the Schofield equation

^g Relative difference between TEE and energy intake

^h Below the protein range of 15 – 25%

Note. REE = resting energy expenditure; TEE = total energy expenditure

Chapter: Discussion

4.1 Overview

Following a burn injury there is a marked increase in resting energy expenditure (REE) which appears dependent on the severity of the injury as measured by total body surface area (TBSA) (Jeschke et al., 2007; Saffle et al., 1985; Wilmore et al., 1975). The current study was conducted in a cohort of male (n = 5) and female (n = 3) burn patients aged 29 – 62 years at the Western Australian (WA) State Adult Burn Unit. The REE for patients with moderate burn injuries was significantly lower than REE of patients with major burn injuries from published studies. The impact of time after a burn injury, age, gender, body mass index (BMI), TBSA and nutritional status on REE could not be adequately analysed as the number of participants was smaller than anticipated. The Schofield and Toronto equations used to predict REE were accurate for moderate burn injuries when compared to measured REE (mREE) using indirect calorimetry. Based on a subjective questionnaire, study participants were in agreement that indirect calorimetry was an acceptable nutritional assessment instrument, supporting its use within this population. This chapter will critically evaluate the research findings in consideration of the original hypotheses, previous publications and the research design.

4.2 Energy expenditure

Ten participants were recruited into the study with six successful indirect calorimetry measurements completed in five participants. The mean (range) mREE was 6494 (5448 – 9639) kJ/day. Using the Schofield equation three participants (60%) were normometabolic and two (40%) were hypermetabolic (**Table 23**). In contrast, Dickerson et al. (2002), in a group of 24 patients with major burn injuries, found that the majority were hypermetabolic. The findings of

the current study suggest that the extent of hypermetabolism in moderate burn injuries is less than that observed for major burn injuries.

4.2.1 Influence of burn size on energy expenditure

In support of hypothesis 1, the mREE of patients with a moderate burn injury from the current study was significantly lower than the mREE of patients with a major burn injury from previous studies ($p < 0.05$) (**Table 22**). In view of this result, the hypothesis is accepted. This finding is consistent with the work of Jeschke et al. (2007), Saffle et al. (1985) and Wilmore et al. (1975) who identified an association between extent of burn injury, as TBSA, and energy expenditure. Increases in immune and inflammatory markers; body temperature; evaporative heat loss; and changes to energy substrate utilisation contribute to the elevation of REE observed in severe burn injuries (Herndon & Tompkins, 2004; Tredget & Yu, 1992). However, others have found no correlation between TBSA and energy expenditure, leading authors to question the strength of the association and the impact of other variables on metabolism following a burn injury (Dickerson et al., 2002; Mancusi-Ungaro et al., 1992; Noordenbos et al., 2000).

Noordenbos et al. (2000) found no correlation between TBSA and REE in a cohort of major burn patients (mean TBSA 44%). TBSA was compared to the extent of hypermetabolism, whereby REE pre-burn was determined using the Harris-Benedict equation. The Harris-Benedict equation is known to overestimate REE to varying degrees dependent of gender, age and body composition (Frankenfield et al., 1998; Owen, 1988). Moreover, visual analysis of graphical data indicates that the TBSA for the Noordenbos et al. (2000) cohort ranged from 15 to 90% and did not include small and moderate burn injuries which may have contributed to the lack of observed association between TBSA and REE. Dickerson et al. (2002) applied similar methodology to Noordenbos et al. (2000) and similarly found no correlation between

TBSA and REE. As with Noordenbos et al. (2000), Dickerson et al. (2002) used the Harris-Benedict equation to compare the increase in REE experienced following a burn injury to TBSA and included only patients with a major burn injury (TBSA range 20 – 80%).

Mancusi-Ungaro et al. (1992) investigated a cohort of 12 moderate and major burn injuries where three participants had a TBSA < 15% and found no correlation between TBSA and REE. Two out of the three participants with a TBSA < 15% had an REE equivalent or greater to their counterparts with a 60% TBSA. These participants experienced unfavourable clinical outcomes including loss of weight, hypoalbuminemia and death secondary to congestive heart failure (n = 1). As such, the elevated REE observed by Mancusi-Ungaro et al. (1992) for moderate burn injuries may have been related to compromised nutritional and medical status, independent of TBSA. In a major burn cohort, Shields et al. (2013) found that TBSA was the largest contributing factor when compared to age, height, pre-burn weight and room temperature. However, this was a moderately strong relationship ($r^2 = 0.45$). This suggests that variables, or a combination of variables beyond TBSA, contribute to the hypermetabolism observed following a burn injury. No obvious trend between TBSA and mREE was observed within the current study in which TBSA ranged from 5.00 to 9.60% (**Figure 10**).

In summary, the REE for patients with moderate burn injuries from the current study was significantly lower than REE previously reported for patients with major burn injuries. These conclusions support the findings of other authors that more severe burn injuries, measured as TBSA, have higher energy expenditure than moderate to low burn injuries (Jeschke et al., 2007; Saffle et al., 1985; Wilmore et al., 1975). This study is limited by the small sample size (n = 6) and the exclusion of major burn injuries. Moreover, the cohort was of optimal nutritional status, evidenced by the Patient Generated-Subjective Global Assess (PG-SGA), hand grip strength

(HGS) and BMI (**Table 29**), which inhibited the exploration of nutritional factors which may contribute to REE, as shown by Mancusi-Ungaro et al. (1992).

4.2.2 Change in energy expenditure following a burn injury

Results were presented as a case study for the participant who underwent two indirect calorimetry measurements (**Table 23**). This participant demonstrated a $\pm 5\%$ change between pre-burn REE and mREE on post-burn day (PBD) three and a 13.5% (744 kJ/day) increase in mREE between PBD three and fifteen. Testing of hypothesis 2 could not be completed due to changes to the study protocol whereby participants were not available for follow up (see section 5.1.5). Therefore, no conclusions regarding the change in energy expenditure over time for moderate burn injuries can be drawn. No literature describing the time course of REE for moderate burn injuries was identified by the researcher. Several studies have examined major burn injuries and found that maximal REE typically occurs within the first 20 days following burn injury after which a gradual and prolonged decrease in REE is observed (Hart et al., 2000; Khorram-Sefat, Behrendt, Heiden, & Hettich, 1999; Milner et al., 1994; Saffle et al., 1985).

In a cohort of patients with major burn injuries (TBSA range 20 – 91%), Khorram-Sefat et al. (1999) found that the mean maximal REE was achieved at PBD five and was 55% of the predicted pre-burn REE. The maximal REE plateaued from PBD five to nineteen, after which a gradual decline towards predicted pre-burn REE, estimated using the Harris-Benedict equations, was observed. Patients with more severe injuries, such as sepsis and multiple-organ failure, experienced a longer period of maximal REE, up to 45 days, reflecting increased and prolonged metabolic demands (Tredget & Yu, 1992). A greater rise in REE was observed in participants assessed as a higher mortality risk compared to those of a lower risk at 59% and

49%, respectively. This observation supports the conclusion that the more severe the injury the greater the metabolic demands and therefore, the greater and longer the elevation in REE.

Saffle et al. (1985) reported that maximal mean REE was achieved at PBD 10.4 (range 1 – 27 days) in a cohort of moderate and major burn patients. REE was observed to gradually decline until hospital discharge where it remained elevated at 24% (- 34 – 88%) of the pre-burn REE, calculated using the Harris-Benedict equations. Saffle et al. (1985) provided no further analysis of change in REE over time based on TBSA for comparison with the current study. PBD was shown to be inversely correlated with the mean maximal REE by Milner et al. (1994) in a cohort of patients with major burn injuries (TBSA range 21 – 88.25%). This correlation was strongest after PBD 30 ($r = -0.673$, $p < 0.001$) with a weaker non-significant correlation observed during the first 30 days following a burn injury ($r = -0.254$, $p = 0.072$). Within the same cohort, TBSA was found to be significantly correlated to REE during the first 30 PBD ($r = 0.587$, $p < 0.001$) and after PBD 30 ($r = 0.454$, $p < 0.001$), although there was a marginally stronger relationship during the first 30 days. Further analysis by the authors found that PBD, when combined with TBSA, accounted for only 40% of the variation observed in the REE. This provides further evidence that multiple factors are responsible for the variation in REE of individuals with burn injuries.

In the current study, a 3.85% (223 kJ/day) decrease in REE was observed between pre-burn REE, estimated using the Harris-Benedict equation, and PBD three for the female participant for which data were collected. This finding is inconsistent with prior studies which suggest that a burn injury is associated with an increase in REE (Khorram-Sefat et al., 1999; Saffle et al., 1985). Use of the Harris-Benedict equation may have resulted in an overestimation of pre-burn REE as the equations are known to systematically overestimate by up to 15% for females (Owen, 1988). However, a clinically insignificant increase of 0.2% (11 kJ/day) was observed

between pre-burn REE using the Schofield equation and PBD three. While the Schofield equation is similarly known to overestimate REE (Ferrie & Ward, 2007) this finding suggests that patients with a moderate burn injury may not experience increases in REE above pre-burn healthy levels. This finding is limited by the small sample size which cannot eliminate the influence of individual biological variation. A 13.5% (223 kJ/day) increase was observed between PBD three and fifteen for the participant, suggesting that REE increases gradually following a moderate burn injury. This finding is consistent with the literature which shows that maximal REE is reached between PBD five and ten for major burn injuries (Khorram-Sefat et al., 1999; Saffle et al., 1985). However, the small sample size limits the generalising of conclusions. Furthermore, potential error in indirect calorimetry measurements may have contributed to this observation (see section 5.1).

4.2.3 Influence of age, gender and nutritional status on energy expenditure in burn injuries

Descriptive graphical analysis was undertaken to examine the impact of age, gender and BMI on mREE (*Figure 10*). No trends were observed between gender and mREE and between BMI and mREE. A trend towards a higher REE for younger participants (< 40 years) and lower REE for older participants (> 40 years) was apparent but limited by the small sample size. Statistical testing of hypothesis 3, including investigation on the impact of nutritional status on mREE, could not be completed due to the small sample size and the well-nourished status of the cohort.

Gender is considered an important determinant of REE with males reported to have a higher REE than females (Cunningham, 1980; Ireton-Jones et al., 1992). However, when a correction for body composition was applied by Cunningham (1980), the impact of gender on REE was insignificant. This suggests that differences in body composition between the genders, whereby

females typically have a lower muscle mass than males, are responsible for the observed variation in REE (Cunningham, 1980; Ireton-Jones et al., 1992). Similarly, age is considered an important determinant of REE for both healthy individuals and those with a burn injury whereby increasing age is associated with decreasing REE (Ireton-Jones et al., 1992; Shields et al., 2013). Age has been shown as a weak variable of REE in patients with major burn injuries ($r^2 = 0.23$) (Shields et al., 2013). As with gender, the impact of age on REE is associated with changes in body composition (Cunningham, 1980). Cunningham (1980) found that lean muscle mass, calculated using an equation based on weight and age, accounted for 70% of the variability of basal metabolic rate (BMR) observed in healthy adults. Muller et al. (2004) used bioelectrical impedance analysis (BIA) to determine lean muscle mass in a large cohort of healthy participants and confirmed the Cunningham (1980) finding by observing that 61.7% of the variability of REE was secondary to body composition. As such, gender and age can be considered factors which influence body composition, with body composition being the primary determinant of REE.

It was not feasible to obtain indirect measures of body composition using tools such as BIA or air displacement plethysmography in the current study. BMI was calculated as an indicator of body composition. However, no association was observed between BMI and mREE, although the participant with the highest BMI also had the highest mREE (**Figure 10**). As BMI is a limited tool for assessment of body composition (Lee & Nieman, 2013), no conclusions can be drawn from this finding. Those participants who were older were observed to have a lower REE compared to their younger counterparts. This is consistent with other studies for patients with burn injuries who found age to be a high ranking but weak contributor of REE (Shields et al., 2013). The findings of the current study are limited by the small sample size and reliance on BMI for assessment of body composition.

4.2.4 Potential influence of medications on energy expenditure

Medications prescribed to participants were recorded and evaluated for their influence on REE with nicotine identified as increasing REE and analgesia decreasing REE (**Table 17**). One participant was prescribed a 24 hour 14 mg nicotine patch at 0800 hours daily which may have resulted in an elevated REE. Collins et al (1996) found that REE increased by 9.3% compared to 5.2% 140 minutes after smoking high nicotine (8.7 mg nicotine) versus low nicotine cigarettes (4 mg nicotine) ($p < 0.05$). The time taken for REE to return to baseline was not reported nor did the researchers consider the impact of different nicotine delivery method, such as smoking versus patches. However, this finding suggests that the mREE for the participant in the current study may have been artificially increased by the use of a nicotine patch.

Analgesia was prescribed to all study participants prior to indirect calorimetry measurements and may have lowered mREE. Swinamer, Phang, Jones, Grace, and King (1988) demonstrated that REE was reduced by 12.7 to 15% after delivery of morphine in a cohort of critically ill participants. The use of analgesia was frequent and warranted in the current cohort given their burn injuries. However, it may have caused a decrease in mREE by up to 15% which may have minimised a potentially significant post-burn injury increase in REE in the current study (Porter & Cohen, 1996; Swinamer et al., 1988).

4.2.5 Prediction of resting energy expenditure

The mean difference between the pREE using the Schofield and Toronto equations and the mREE for the cohort was within $\pm 10\%$ (**Table 24**), which supports hypothesis 4 of a non-significant difference between predicted and measured REE at a group level. It is concluded that the Schofield and Toronto equations are accurate for predicting REE in patients with

moderate burn injuries at a group level. At an individual, there was wide variation with a percentage difference ranging from -7.76 to 20.51% for the Schofield equations and -5.10 to 28.20% for the Toronto equation. The Schofield equations were accurate to $\pm 10\%$ in 67% of participants and overestimated in the remaining 33% of participants (1,138 kJ/day and 1,270 kJ/day overestimation). The Toronto equation was accurate to $\pm 10\%$ for 50% of participants and overestimated in the remaining 50% (607 kJ/day, 1,565 kJ/day and 1,016 kJ/day overestimation). Therefore, neither equation is acceptable at an individual level. If either equation is used to guide nutrition therapy at an individual level for low to moderate burn patients there is a risk of over delivery of energy. The clinical impact of this potential over-delivery of energy is difficult to interpret due to a lack of published literature on overfeeding in hospitalised patients (Chapman, Peake, & Jones, 2015). Hasson et al. (2011) report $\pm 1,045$ kJ/day as an acceptable margin of error however, state that caution should be taken when applying to hospitalised individuals. Recent critical care nutrition guidelines advise against overfeeding and advocate for regular monitoring but do not provide specific targets (McClave et al., 2016). As such, the cautious use of the Schofield and Toronto equations for the estimation of energy expenditure, in the absence of indirect calorimetry, in patients with moderate to low burn injuries is recommended with monitoring for evidence of overfeeding.

4.2.5.1 Performance of the Schofield equations

In this study the Schofield equations were the most accurate method for predicting mREE by indirect calorimetry for individuals with a moderate burn injury. These equations are endorsed by the Australian and New Zealand Burn Association (ANZBA) (Edgar, 2014) for non-ventilated burn patients and are widely used by Australian practitioners (Ferrie & Ward, 2007; Masters & Wood, 2008). Their popularity is attributed to their simplicity and their representativeness of a culturally diverse Australian population (Ferrie & Ward, 2007). An

injury factor may be required when using the equations with burn patients to account for the expected increase in metabolism (Edgar, 2014; Masters & Wood, 2008). Based on expert opinion, the ANZBA guideline (Edgar, 2014) recommend an injury factor of 10% for < 10% TBSA which, for improved accuracy, was interpreted by the researcher as a 5% factor for TBSA of approximately 5% and 10% for injuries of approximately 10% TBSA (**Table 8**). Conversely, Masters and Wood (2008) recommend an injury factor of 20% for < 10% TBSA based on a survey of practices in Australian and North American burn units. Had an injury factor of 20% been applied to the current study cohort it would have resulted in a marked overestimation of REE. Therefore, this study provides evidence to support the conservative injury factor range for the Schofield equations endorsed by ANZBA for moderate burn injuries.

There are no published studies on the validity of the Schofield equations and associated injury factors for patients with burn injuries. Despite the widespread use of the equations and endorsement by ANZBA (Edgar, 2014) they were not included in a large review examining the accuracy and precision of predictive methods for patients with burn injuries by Dickerson et al. (2002). In critically ill non-burn patients, Reid (2007) concluded that the equations significantly overestimate energy requirements (**Table 31**). Clark and Hoffer (1991), Hasson et al. (2011) and Muller et al. (2004), reported that the Schofield equations significantly over predicted energy requirements when compared to indirect calorimetry for healthy adults (**Table 31**). The equations have an observed energy dependent bias whereby they overestimate at lower energy requirements and underestimate at upper energy requirements (Muller et al., 2004).

In the current study, the mean difference between the Schofield equations and mREE was within $\pm 10\%$. However, pREE was markedly overestimated for two participants (19.33% and 20.51%) (**Table 24**). Further analysis of the data shows that these two participants were within the reference BMI range (23.1 kg/m² and 22.6 kg/m²), while the three participants whose REE was accurately predicted were classified as overweight, with one participant having an adjusted

body weight applied (26.7 kg/m², 26.4 kg/m² and 26.4 kg/m², respectively). The accuracy of the Schofield equation for overweight participants is inconsistent with previous results by Muller et al. (2004) who found that the equations overestimated for normal and overweight but not obese BMI categories for healthy participants (**Table 31**).

The application of the Schofield equations to burn patients is limited as the equations do not include variables known to improve the prediction of energy expenditure such as injury extent (e.g., TBSA), PBD, lean muscle mass or energy intake (Allard et al., 1988; Cunningham, 1980; Rodriguez et al., 2011). Furthermore, the dataset used to develop the Schofield equations is reported to have experienced methodological inconsistencies, including variable room temperature during indirect calorimetry measures causing sweating and shivering in participants, the inclusion of approximately 1000 young male soldiers in the dataset and one third of participants who were considered underweight (BMI < 20kg/m²), which may have affected the accuracy of the equations (Ferrie & Ward, 2007; Muller et al., 2004).

4.2.5.2 Performance of the Toronto equation

The Toronto equation is a recently developed burn injury predictive equation regarded as one of the more accurate equations (Berger, 2008; Rodriguez et al., 2011). The Toronto equation accounts for body temperature, PBD, extent of burn injury, previous energy intake and pre-burn healthy REE, which have all been shown to affect REE (Allard et al., 1988; Berger, 2008). However, these variables together account for only 67% of the variation observed in REE as evidenced by the r^2 value, suggesting that other unidentified factors influence energy expenditure in patients with burn injuries (Allard et al., 1990). The equation is applicable to a wide range of burn injuries as the population in which it was developed had a TBSA range between 7 to 90% (Allard et al., 1988).

The accuracy of the Toronto equation compared to mREE is summarised in **Table 30**. Of the six studies that evaluated the Toronto equation, four reported no difference between pREE and mREE, one observed the equation to underestimate and one observed the equation to overestimate, suggesting that the equation performs well for individuals with major burn injuries. One of the summarised studies (Royall et al., 1994) included two participants with a TBSA burn injury < 20% and observed no difference between pREE and mREE for the cohort (mean TBSA 36.7%).

The current study found that the Toronto equation was accurate for three out of six participants with values within $\pm 10\%$ of the mREE and overestimated for the remaining three participants (11.14%, 15.46% and 28.20%) (**Table 24**). This finding suggests that the Toronto equation has a trend towards overestimation of REE in a group of patients with moderate burn injuries. One limitation of the Toronto equation is that it was developed in a cohort of predominately major burn patients and validated in a small cohort of exclusively ventilated major burn patients (TBSA 30 – 90% TBSA) (Allard et al., 1990) which may contribute to this finding.

4.2.5.3 Performance of the Harris-Benedict equations

The Harris-Benedict equations are considered the classical method to estimate energy requirement for individuals with a burn injury (Berger, 2008; Masters & Wood, 2008). The current study found the equations overestimated REE by 8.04 to 76.77% when applied to a moderate burn cohort with a 20% injury factor (**Table 24**). This finding has similarly been observed by others and the validity of the equation for burn populations has been questioned (Dickerson et al., 2002; Garrel & de Jonge, 1993; Stucky, Moncure, Hise, Gossage, & Northrop, 2008; Wall-Alonso et al., 1999). A potential source of variation is the wide range of injury factors applied to the Harris-Benedict equation in order to account for the increased

metabolism observed with burn injury. Dickerson et al. (2002) identified more than ten different injury factors used with the equations within the literature, thus highlighting the difficulty in quantifying the extent of hypermetabolism observed in individuals following a burn injury.

The accuracy of the Harris-Benedict equations for burn and non-burn cohorts is summarised in **Table 30**. Of the six studies which evaluated the Harris-Benedict equations for individuals with burn injuries, three overestimated (Clark & Hoffer, 1991; Muller et al., 2004; Wall-Alonso et al., 1999) and one reported no significant difference between pREE and mREE (Shields et al., 2013). Garrel and de Jonge (1993) observed the Harris-Benedict equations were accurate to within $\pm 10\%$ of the mREE for 27% of participants. Another study (Dickerson et al., 2002) reported that the equations underestimated when a 23% injury factor was applied and reported no difference with a 50% injury factor. Variation in the application of injury factors is observed between studies.

Table 30

Summary of studies reporting the performance of predictive equations compared to measured resting energy expenditure

Citation	Cohort characteristics	pREE ^b	mREE	Comparison of pREE to mREE	Conclusions
		Mean ± SD (kJ/day)	Mean ± SD (kJ/day)		
Allard et al. (1990)	10 ventilated burn patients 9M 1F 34.3 ± 3.7 yrs (19 – 55 yrs) TBSA 49.1 ± 5.5% (30 – 90%)	Toronto 10 625 ± 238	10 604 ± 359 ^a	Toronto No significant difference (NS)	The Toronto equation accurately predicts REE for adult major burn patients.
Clark and Hoffer (1991)	29 healthy non-burn participants 29M 0F 24.4 ± 3.3 years (18 – 33 years)	Schofield 7495 ± 623 Harris-Benedict 7578 ± 685	6868 ± 619 ^a	Schofield Significant overestimation (p < 0.05) Harris-Benedict Significant overestimation (p < 0.05)	The Schofield and Harris-Benedict equations overestimate REE for healthy adult males.
Dickerson et al. (2002)	24 ventilated and spontaneous breathing burn patients 19M 5F 36 ± 12 yrs TBSA 37 ± 15% (20 – 80%)	NR for each equation	11 620 ± 2403 ^a	Ireton Jones (spontaneous breathing version) <ul style="list-style-type: none"> No significant difference (NS) Unbiased (95% CI -3361 – 1446 kJ/d)^e Not precise (mean error 18 ± 22%)^f Toronto <ul style="list-style-type: none"> Significant underestimation (p = 0.001) Biased (95% CI -3662 – -1141 kJ/d)^e Not precise (mean error 26 ± 21%)^f 	For adult major burn patients: <ul style="list-style-type: none"> The Ireton Jones equation is unbiased but imprecise The Toronto equation underestimates REE

^a mREE determined using indirect calorimetry

^b pREE determined using a predictive equation (Toronto, Schofield, Harris-Benedict or Ireton-Jones) or energy-per-kilogram formula

^c mREE determined using doubly labelled water

^d Injury factors: 50% for < 15% TBSA; 75% for 15 – 30% TBSA; 200% for 30 – 50%; 220% for > 40% TBSA

^e An equation is considered unbiased if the 95% CI includes zero (Dickerson et al., 2002)

^f An equation is considered precise if the 95% CI for the root mean squared prediction error is within 15% of the mREE (Dickerson et al., 2002)

^g Adjusted for age, sex, BMI and race

^h Using a Bland-Altman plot

Note. M = male; F = female; mREE = measured resting energy expenditure; pREE = predicted resting energy expenditure; TBSA = total body surface area NS = not significant; NR = not reported; BMI = body mass index; yrs = years

Table 30 (continued)

Summary of studies reporting the performance of predictive equations compared to measured resting energy expenditure

Citation	Cohort characteristics	pREE ^b Mean ± SD (kJ/day)	mREE ^a Mean ± SD (kJ/day)	Comparison of mREE and pREE	Conclusions
Dickerson et al. (2002) continued.	24 ventilated and spontaneous breathing burn patients 19M 5F 36 ± 12 yrs TBSA 37 ± 15% (20 – 80%)	NR for each equation	11 620 ± 2403 ^a	<p>130 kJ/kg/day</p> <ul style="list-style-type: none"> Significant difference (p = 0.05) Unbiased (95% CI -2391 – 389kJ/d)^e Not precise (mean error 23 ± 29%)^f <p>146 kJ/kg/day</p> <ul style="list-style-type: none"> No significant difference (NS) Unbiased (95% CI -1129 – 1864 kJ/d)^e Not precise (mean error 23 ± 36%)^f <p>167 kJ/kg/day</p> <ul style="list-style-type: none"> Significant difference (p = 0.01) Biased (95% CI 447 – 3716 kJ/d)^e Not precise (mean error 27 ± 46%)^f <p>Harris-Benedict (IF 23%)</p> <ul style="list-style-type: none"> Significant difference (p = 0.01) Biased (CI 95% -3500 – -1308 kJ/d)^e Not precise (mean error 26 ± 17%)^f <p>Harris-Benedict (IF 50%)</p> <ul style="list-style-type: none"> No significant difference (NS) Unbiased (CI 95% 1492 – 803 kJ/d)^e Not precise (mean error 19 ± 24%)^f 	For adult major burn patients: <ul style="list-style-type: none"> The 130 kJ/kg/day range is unbiased and not precise The 146 kJ/kg/day range is unbiased and not precise The 167 kJ/kg/day range overestimates REE Harris-Benedict (23% IF) underestimates REE Harris-Benedict (50% IF) is unbiased and not precise

^a mREE determined using indirect calorimetry

^b pREE determined using a predictive equation (Toronto, Schofield, Harris-Benedict or Ireton-Jones) or energy-per-kilogram formula

^c mREE determined using doubly labelled water

^d Injury factors: 50% for < 15% TBSA; 75% for 15 – 30% TBSA; 200% for 30 – 50%; 220% for > 40% TBSA

^e An equation is considered unbiased if the 95% CI includes zero (Dickerson et al., 2002)

^f An equation is considered precise if the 95% CI for the root mean squared prediction error is within 15% of the mREE (Dickerson et al., 2002)

^g Adjusted for age, sex, BMI and race

^h Using a Bland-Altman plot

Note. M = male; F = female; mREE = measured resting energy expenditure; pREE = predicted resting energy expenditure; TBSA = total body surface area NS = not significant; NR = not reported; BMI = body mass index; yrs = years

Table 30 (continued)

Summary of studies reporting the performance of predictive equations compared to measured resting energy expenditure

Citation	Cohort characteristics	pREE ^b Mean ± SD (kJ/day)	mREE ^a Mean ± SD (kJ/day)	Comparison of mREE and pREE	Conclusions
Garrel and de Jonge (1993)	19 ventilated and spontaneous breathing burn patients 11M 8F 33.2 ± 15.5 yrs (20 – 74 yrs) TBSA 40 ± 16% (20 – 83%)	NR for each equation	9744 ± 3110 ^a	Harris-Benedict (IF 200%) pREE within ± 10% the mREE in 27% of participants Toronto mREE is 24% higher than pREE (NR)	The Harris-Benedict equations, with a 200% IF, is accurate in 27% of the adult major burn participants. The Toronto equation was 24% higher than REE for the adult major burn participants.
Hasson et al. (2011)	362 healthy non-burn participants 186M 176F 36.0 ± 12.8 yrs (18 – 60 yrs)	Harris-Benedict 6785 ± 24 Schofield 6868 ± 20	6746 ± 51 ^a	Harris-Benedict • No significant difference (NS) ^g • 57.6% were ± 10% mREE ^h Schofield • Significant overestimation (p < 0.01) ^g • 55.5% were ± 10% mREE ^h	The Harris-Benedict equation accurately predicts REE for healthy adults. The Schofield equation overestimates REE for healthy adults.
Muller et al. (2004)	1059 non-burn adult participants 410M 649F 44.1 ± 17.4 yrs (NR) BMI 26.8 ± 7.1 kg/m ² (NR)	Schofield 6760 ± 1360 Harris-Benedict pREE not reported	6650 ± 1540 ^a	Schofield • Significant overestimation BMI < 18 (p < 0.001); BMI 18 – 25 (p < 0.05); BMI 25 - 30 (p < 0.001) • No significant difference BMI > 30 (NS) Harris-Benedict • Significant overestimation for BMI < 18 (p < 0.001) • No significant difference for BMI 18 – 25; BMI 25 - 30; BMI > 30 (NS)	The Schofield equation overestimates REE for adult healthy individuals except those with a BMI > 30 kg/m ² . The Harris-Benedict equation accurately predicts REE for adult healthy individuals except those with a BMI < 18 kg/m ² .

^a mREE determined using indirect calorimetry

^b pREE determined using a predictive equation (Toronto, Schofield, Harris-Benedict or Ireton-Jones) or energy-per-kilogram formula

^c mREE determined using doubly labelled water

^d Injury factors: 50% for < 15% TBSA; 75% for 15 – 30% TBSA; 200% for 30 – 50%; 220% for > 40% TBSA

^e An equation is considered unbiased if the 95% CI includes zero (Dickerson et al., 2002)

^f An equation is considered precise if the 95% CI for the root mean squared prediction error is within 15% of the mREE (Dickerson et al., 2002)

^g Adjusted for age, sex, BMI and race

^h Using a Bland-Altman plot

Note. M = male; F = female; mREE = measured resting energy expenditure; pREE = predicted resting energy expenditure; TBSA = total body surface area NS = not significant; NR = not reported; BMI = body mass index; yrs = years

Table 30 (continued)

Summary of studies reporting the performance of predictive equations compared to measured resting energy expenditure

Citation	Cohort characteristics	pREE ^b Mean ± SD (kJ/day)	mREE ^a Mean ± SD (kJ/day)	Comparison of mREE and pREE	Conclusions
Reid (2007)	27 critically ill ventilated non-burn patients 13M 14F 57 ± 15.6 yrs (range NR)	NR for each equation	8581 ± 1860 ^a	Schofield (IF 30%) Mean bias 355 ± 117 kJ/d (limits of agreement -2817 – 3528 kJ/d) (p < 0.0001) ^g Harris-Benedict (IF 30%) Mean bias 464 ± 116 kJ/d (limits of agreement -2675 – 3603 kJ/d) (p < 0.0001) ^g 105 kJ/kg/day Mean bias 765 ± 111 kJ/d (limits of agreement -2236 – 4059 kJ/d) (p < 0.0001) ^g	The Schofield and Harris-Benedict equation and 105 kJ/kg/day range are unreliable for the prediction of REE in adult critically ill non-burn patients.
Royall et al. (1994)	20 ventilated patients 17M 3F 44.4 ± 3.3 yrs (range NR) TBSA 36.7 ± 4.2% (10 – 90%)	Toronto 9158 ± 346 Harris-Benedict (IF 20%) 13 083 ± 343	10 416 ± 502 ^a	Toronto No significant difference (NS) Harris-Benedict (IF 200%) Significant overestimation (p < 0.005)	The Toronto equation accurately predicts REE for moderate and major burn patients. The Harris-Benedict equation with a 200% IF overestimates REE for adult moderate and major burn patients.

^a mREE determined using indirect calorimetry

^b pREE determined using a predictive equation (Toronto, Schofield, Harris-Benedict or Ireton-Jones) or energy-per-kilogram formula

^c mREE determined using doubly labelled water

^d Injury factors: 50% for < 15% TBSA; 75% for 15 – 30% TBSA; 200% for 30 – 50%; 220% for > 40% TBSA

^e An equation is considered unbiased if the 95% CI includes zero (Dickerson et al., 2002)

^f An equation is considered precise if the 95% CI for the root mean squared prediction error is within 15% of the mREE (Dickerson et al., 2002)

^g Adjusted for age, sex, BMI and race

^h Using a Bland-Altman plot

Note. M = male; F = female; mREE = measured resting energy expenditure; pREE = predicted resting energy expenditure; TBSA = total body surface area NS = not significant; NR = not reported; BMI = body mass index; yrs = years

Table 30 (continued)

Summary of studies reporting the performance of predictive equations compared to measured resting energy expenditure

Citation	Cohort characteristics	pREE ^b Mean ± SD (kJ/day)	mREE ^a Mean ± SD (kJ/day)	Comparison of mREE and pREE	Conclusions
Shields et al. (2013)	31 ventilated and spontaneous breathing burn patients 24M 7F 46 ± 19 yrs (19 – 85 yrs) TBSA 48 ± 21% (20 – 95%)	Harris-Benedict (IF 50%) 10 316 ± 1643 125 kJ/kg/day 6893 ± 1317 146 kJ/kg/day 8042 ± 1534 167 kJ/kg/day 9192 ± 1756	10 550 ± 3085 ^a	Harris-Benedict (IF 50%) No significant difference (NS) 125 kJ/kg/day, Significant underestimation (p < 0.05) 146 kJ/kg/day Significant underestimation (p < 0.05) 167 kJ/kg/day Significant underestimation (p < 0.05)	The Harris-Benedict equations with a 50% IF accurately predict REE for adult major burn patients. All energy-per-kilogram method underestimates REE for adult major burn patients.
Stucky et al. (2008)	9 ventilated obese burn patients Gender NR 45.42 ± 17.99 yrs (range NR) TBSA 46.85 ± 26.35% (range NR)	Harris-Benedict (IF 20%) 9807 ± 1548	9187 ± 2051 ^a	Harris-Benedict (IF 20%) Mean bias -614 ± 1918 kJ/d ^g	The Harris-Benedict equations overestimate REE for adult obese major burn patients.

^a mREE determined using indirect calorimetry

^b pREE determined using a predictive equation (Toronto, Schofield, Harris-Benedict or Ireton-Jones) or energy-per-kilogram formula

^c mREE determined using doubly labelled water

^d Injury factors: 50% for < 15% TBSA; 75% for 15 – 30% TBSA; 200% for 30 – 50%; 220% for > 40% TBSA

^e An equation is considered unbiased if the 95% CI includes zero (Dickerson et al., 2002)

^f An equation is considered precise if the 95% CI for the root mean squared prediction error is within 15% of the mREE (Dickerson et al., 2002)

^g Adjusted for age, sex, BMI and race

^h Using a Bland-Altman plot

Note. M = male; F = female; mREE = measured resting energy expenditure; pREE = predicted resting energy expenditure; TBSA = total body surface area NS = not significant; NR = not reported; BMI = body mass index; yrs = years

Table 30 (continued)

Summary of studies reporting the performance of predictive equations compared to measured resting energy expenditure

Citation	Cohort characteristics	pREE^b Mean ± SD (kJ/day)	mREE^a Mean ± SD (kJ/day)	Comparison of mREE and pREE	Conclusions
Tancheva et al. (2005)	20 ventilated burn patients 17M 3F 37.83 ± 10.86 yrs (21 – 58 yrs) TBSA 34.27 ± 11.55% (20 – 60%)	Toronto 10 809 ± 823	9672 ± 581 ^a	Toronto No significant difference (NS)	The Toronto equation accurately predicts REE for adult major burn patients.
Wall-Alonso et al. (1999)	13 non-ventilated patients 9M 4F 40 ± 13 yrs (22 – 62 yrs) TBSA 38 ± 23% (15 – 80%)	Harris-Benedict^d 11 704 ± 1546 Toronto 11 035 ± 1337 kJ/day	9609 ± 1425 ^c	Harris-Benedict^d Significant overestimation by 16.5 ± 12.9% (p < 0.05) Toronto Non-significant overestimation of 10 ± 15% (NS)	The Harris-Benedict equations significantly overestimate REE for adult major burn patients. The Toronto equation accurately predicts REE for adult major burn patients.

^a mREE determined using indirect calorimetry

^b pREE determined using a predictive equation (Toronto, Schofield, Harris-Benedict or Ireton-Jones) or energy-per-kilogram formula

^c mREE determined using doubly labelled water

^d Injury factors: 50% for < 15% TBSA; 75% for 15 – 30% TBSA; 200% for 30 – 50%; 220% for > 40% TBSA

^e An equation is considered unbiased if the 95% CI includes zero (Dickerson et al., 2002)

^f An equation is considered precise if the 95% CI for the root mean squared prediction error is within 15% of the mREE (Dickerson et al., 2002)

^g Adjusted for age, sex, BMI and race

^h Using a Bland-Altman plot

Note. M = male; F = female; mREE = measured resting energy expenditure; pREE = predicted resting energy expenditure; TBSA = total body surface area NS = not significant; NR = not reported; BMI = body mass index; yrs = years

Wall-Alonso et al. (1999) applied factors ranging from 50 to 120% dependent on the TBSA, which likely contributed to the overestimation as others (Dickerson et al., 2002) have shown that injury factors within these ranges are excessive. Shields et al. (2013) applied a 50% injury factor to the entire cohort and found no significant difference between the pREE and the mREE. This trend was observed within each TBSA subgroup (e.g., 0 – 32%, 33 – 65% and 66 – 100% TBSA). Notably, the authors found no difference between Harris-Benedict with a 50% injury factor and mREE in the sub group 0 to 32% TBSA ($p = 0.10$), suggesting that it is applicable for moderate burn injuries. However, this finding is limited as further analysis of the study reveals that there were no burn injuries < 20% TBSA included in the cohort. The current study applied a 20% injury factor endorsed by ANZBA guidelines (Edgar, 2014) and found that the Harris-Benedict equation overestimated by $32.14 \pm 30.79\%$. When the Harris-Benedict equation without an injury factor was used to estimate pre-burn healthy REE (**Table 23**) there was no clinically significant difference between mREE and pre-burn REE (-1.16% or -77 kJ/day).

Stucky et al. (2008) found that the Harris-Benedict equations overestimated requirements when applied to a cohort of obese major burn patients (**Table 30**). Further analysis of the current study identified that the Harris-Benedict equation accurately estimated REE for three out of six participants (8.04%, 8.92% and 9.70%) and overestimated for the remaining three (24.62%, 64.80% and 79.77%). All participants where the Harris-Benedict equation was accurate had a BMI within the overweight range, with an adjusted body weight applied for one participant, and two participants with a BMI within the reference range were found to have the largest overestimation of REE (64.80% and 76.77%). This suggests that the Harris-Benedict equations perform most accurately for overweight patients with a moderate burn injury. This is contrary to conclusions drawn by Stucky et al. (2008). However, Stucky et al. (2008) applied a stricter criteria for accuracy than the $\pm 10\%$ used in the current study. The finding that the Harris-

Benedict equation performs better in overweight individuals is supported by Frankenfield et al. (1998) who noted that the original Harris-Benedict equations included 5.4% overweight and 2.5% obese subjects and suggests that this improved the equations accuracy within these populations.

4.2.5.4 Performance of the Ireton-Jones equations

The Ireton-Jones equation for spontaneously breathing patients was not accurate in the current study with a mean difference of 18.80% from the mREE, with one participant out of five observed to have their REE accurately predicted (within 5.46%). REE was underestimated for one participant (-12.79%) and overestimated for four participants ranging from 18.30 to 35.98% (**Table 24**). Studies have focussed on the validity of the ventilated Ireton-Jones equation for burn and critically ill patients rather than the spontaneously breathing version (Frankenfield, Smith, & Cooney, 2008; Reid, 2007). However, a review by Dickerson et al. (2002) included the spontaneously breathing version of the equation and found no significant difference when compared to the mREE in patients with major burn injuries (**Table 30**).

The spontaneously breathing Ireton-Jones equation does not include a factor for burn injury severity as no correlation between presence of a burn injury and mREE was identified for spontaneously breathing patients by Ireton-Jones et al. (1992). However, several years earlier Allard et al. (1988) had reported that TBSA was significantly correlated with mREE ($p < 0.001$) in a population of both spontaneously breathing and ventilated patients. As previous researchers have identified TBSA as a contributing factor to REE (Shields et al., 2013), the absence of burn TBSA may be a limitation of the Ireton-Jones equation. Furthermore, the equation was derived and then validated in a mixed cohort of trauma and burn injuries in which the mean TBSA was $41 \pm 19\%$ (3 – 75%) and $41 \pm 23\%$ (7 – 84%), respectively. As such, the

equation may not be accurate for patients with moderate burn injuries, reflected in the results of the current study.

4.2.5.5 Performance of the energy-per-kilogram formulae

The energy-per-kilogram formulae for predicting REE were inaccurate when applied to moderate burn injuries in the current study. Both the lower and upper bounds of the range (100 kJ/kg/day and 125 kJ/kg/day) overestimated REE by 15.03% and 43.79%, respectively (**Table 24**). Dickerson et al. (2002) found that none of the energy-per-kilogram ranges cited within the literature for burn injuries were precise (**Table 30**). Ireton-Jones and Jones (2002) reported that the mean energy-per-kilogram observed in a mixed cohort of trauma and major burn patients was 121 kJ/kg/day (38 – 255 kJ/kg/day). However, this correlated poorly with the mREE ($r = 0.46$) and overestimated energy requirements in 81% of the cohort. In the current study the mean energy-per-kilogram for the cohort was 86 (75 – 95) kJ/kg/day which is significantly lower than the recommended range of 100 to 125 kJ/kg/day (Edgar, 2014). While this range could be proposed as a more accurate formula to estimate REE in the current group of moderate burn injuries, the use of energy-per-kilogram formulae is not recommended as they do not consider variables of influences (Dickerson et al., 2002; Ireton-Jones & Jones, 2002).

4.2.6 Patient acceptability of indirect calorimetry measurements

This study used a 14 item questionnaire to explore patient perspectives of indirect calorimetry measurements. In support of hypothesis 5, all study participants who completed the questionnaire reported that the indirect calorimetry procedure was acceptable. In view of this result, the hypothesis is accepted. Participants were found to agree with all statements except

the acceptability of indirect calorimetry for routine testing in burn patients where 60% (n = 3) agreed and 40% (n = 2) indicated a neutral position.

Participants all agreed that the duration and timing (< 30 minutes, before breakfast) for the indirect calorimetry measurements were appropriate. De Waele et al. (2013) found that the mean time taken to complete an indirect calorimetry measurement was 35 minutes, comprising 9.5 minutes of data input and preparing the participant, 23.0 minutes for the actual measurement and 2.9 minutes for data processing. The authors concluded that this was a clinically appropriate length of time to spend on indirect calorimetry from a practitioner perspective. No data on the patient experience was collected as they were sedated patients in intensive care.

The mean duration of indirect calorimetry measurement for the current study was 23 ± 3 minutes. Additional time was required to complete the calibration, data entry, prepare the patient and process data. Although not recorded at the time, the researcher indicated that the warm up of the system took 30 minutes followed by a calibration of between 5 and 20 minutes. The calibration of the system was often lengthy, up to 20 minutes, due to difficulties with the equipment. Data entry and preparing the participant were efficient and estimated to take no more than 5 minutes. The inability of the Ultima CPX to automatically calculate a steady state meant that measurements had to be run for a pre-defined length of time, at least 20 minutes and no more than 30 minutes.

All participants of the current study found the time of day to be convenient although several participants had to be woken by nursing staff for the measurement. The early morning indirect calorimetry measurements were ideal for this research project as it ensured that the participants met fasting requirements, were relaxed and that routine medical treatments and therapies were avoided. However, several participants fell asleep during the measurement for short periods

which may have reduced their REE (Feurer & Mullen, 1986). While suitable for this research project, early morning measurements may be impractical for routine care and indirect calorimetry throughout the day may be more realistic. In a review of indirect calorimetry practices Fullmer et al. (2015) concluded that measures over a 24 hour period resulted in a small but clinically acceptable 3 to 5% variation.

Participants reported that the testing environment conditions were all adequate. These included the room temperature, privacy, and absence of pain, their comfort level, the need to empty their bladder and bowels, their ability to breathe, and remain relaxed and still. This reported level of agreement for the participants ability to remain still and relaxed is inconsistent with the researchers own observations in which several participants appeared to have difficulty lying still and would frequently move their arms and legs. All participants indicated that they would be willing to repeat the indirect calorimetry measurement although only three agreed with the measurement being routinely used for burn care. Written comments (n = 2) suggested using less invasive and quicker methods such as predictive equations: “...*I circled neutral because research could be done on a few people to get a range for weight/ height etc then go off that, save everybodys time...*”

Two participants commented that the face tent could be altered to improve comfort. In particular, one participant advocated for a wider head band and another for an improved fit for those with a beard. The researcher is in agreement with these comments as eight individuals who met the inclusion criteria for the study were unable to participate due to the presence of facial burn or trauma which impeded their ability to wear the face tent. Feuerer and Mullen (1986) report that an alternative to the face tent, the canopy hood system, is well tolerated by participants and is conducive to longer measurements. No canopy system was available for the Ultima CPX and is a limitation of this equipment.

Overall, participants agreed that the indirect calorimetry measurement was acceptable. This is an important finding as it is the first study in burns management to explore the indirect calorimetry experience from the patient's perspective. This result extends previous studies indicating that indirect calorimetry is an accurate and time efficient tool for individuals with a burn injury. The experience for the participants and therefore accuracy of the REE measurement could be improved by using a more comfortable gas collection system such as a canopy hood which is available with other indirect calorimeters.

4.3 Dietary intake

4.3.1 Energy balance

The mean daily energy intake for the study cohort was 9703 (6496 – 14 131) kJ determined using a 24 hour dietary recall. When compared to total energy expenditure (TEE) there was a mean energy deficit of 47 kJ/day (**Table 29**) which is considered a clinically insignificant quantity (Hasson et al., 2011). However, there was wide individual variation with four participants out of seven experiencing an energy deficit ≥ 1500 kJ/day. Prolonged energy deficit following a burn injury has been shown to cause loss of weight, impaired immune function, reduced wound healing and increased risk of infection (Rodriguez et al., 2011). However, the accuracy of the estimated energy deficit is influenced by several factors including the application of an activity factor to determine TEE and the accuracy of the 24 hour recall method.

An activity factor of 50% was applied to the REE, determined by either indirect calorimetry or the Schofield equation, in order to estimate TEE. The 50% activity factor was derived from Ferrie and Ward (2007) and applied to the cohort based on estimated physical activity duration, type and intensity as described by the FSH Burn Unit physiotherapist. However, this activity

factor may have been an overestimation and lead to an overrepresentation of participants with an energy deficit. Burn publications have focussed on suitable activity factors for sedated or critically ill patients with a lack of documentation regarding energy expenditure during intensive regular physiotherapy, such as that undertaken by the current cohort. Royall et al. (1994) determined that in a critically ill sedated major burn population an activity factor of 20% should be used to achieve TEE, noting a wide variation between individuals. During a physiotherapy session, burn patients on average were observed to expend 24% more energy when compared to rest, with the mean length of time for a physiotherapy session of 0.9 ± 0.2 hours per day. For all daily activities, including physiotherapy, a 7% increase in REE was observed post-activity. The current cohort was estimated to participate in 30 minutes walking each day as well as a 30 minute gym session five times per week, which is greater and of higher intensity than that observed by Royall et al. (1994). Other daily activities such as positioning within the bed, wound dressing changes, agitation and family visits all resulted in an increase in energy expenditure above REE in the Royall et al. (1994) cohort. Similarly, Wall-Alonso et al. (1999) applied a 40% activity factor for individuals participating in moderate physical activity. Therefore, an activity factor of 50% was selected to account for the additional activities undertaken by study participants in the current study.

The time and cost efficiency of the 24 hour recall makes it a frequently used dietary assessment method. However, it relies on respondent memory which can lead to omission and commission of foods and beverages resulting in either under- or overreporting (Slimani et al., 2000). Use of sedation and analgesia can further impact an individual's ability to accurately recall items and quantities and may have influenced the estimated energy intake of the current study. Poslusna, Ruprich, de Vries, Jakubikova, and van't Veer (2009) reported that increasing BMI; being older; being female; being from a lower socio-economic status; and smoking and dieting increases the probability of underreporting. However, the 24 hour recall is an accepted dietary

assessment tool and was appropriate for the current study to provide an estimation of energy intake in hospitalised patients with a burn injury.

The gold standard for determination of TEE is the doubly labelled water method. While it has been applied with burn populations (Goran, Peters, Herndon, & Wolfe, 1990; Wall-Alonso et al., 1999) it was beyond the scope of this project. An alternative is the use of a prospective physical activity log to record physical activity. Such a log would have improved the accuracy of selecting an activity factor and would have enabled a tailored activity factor to be applied to each individual participant.

4.3.2 Protein intake

The mean protein intake was 91 (58 – 139) g/day; four participants were within the protein range of 15 to 25%, two were below and three above (**Table 30**). Long term inadequate protein intake can lead to loss of lean muscle mass with increased risk of morbidity and mortality (Edgar, 2014). However, both participants below the protein range were within 4 g of the lower boundary which is clinically insignificant. One participant exceeded the upper recommended protein bound by 24 g/day. Long term excessive protein intake, defined as > 3 g/kg/day or > 25% total energy intake, can lead to renal insufficiency (Edgar, 2014). However, further analysis of this participant indicated that their protein intake equated to 1.5 g/kg/day and they had a 9.6% TBSA injury, which is not inconsistent with ANZBA recommendations of 1.0 to 1.5 g/kg/day (Edgar, 2014). Australian practice guidelines recommend that protein contributes between 15 and 25% of energy intake (Masters & Wood, 2008). The mean protein contribution for the current study was 15% with three participants below the range (9%, 11% and 11%) (**Table 30**). Research is inconclusive regarding the optimal quantity of protein for burn patients (Edgar, 2014). The current study found that no participants were at risk of inadequate protein

intake when examining the protein intake in grams, although the protein contribution to total energy intake was below the specified range. The impact of individual daily variation cannot be eliminated and subsequent daily analysis is recommended. The gold standard for determination of protein status is urinary nitrogen analysis which provides accurate data on protein requirements (Lee & Nieman, 2013) but was beyond the scope of this project.

Chapter: Limitations, Conclusions and Recommendations

5.1 Limitations

The aim of this study was to determine and explore the resting energy expenditure (REE) of individuals with a moderate burn injury using indirect calorimetry. However, unexpected challenges were encountered in the execution of the study protocol resulting in lower than anticipated participant recruitment and the need to discard four indirect calorimetry measurements (**Table 19**). These challenges included the determination and achievement of a steady state, the use of the Ultima CPX for indirect calorimetry measurements and the small number of participants available for recruitment.

5.1.1 Determination and achievement of a steady state

This study developed and employed an algorithm for the identification of a steady state during indirect calorimetry measurements based on previously published studies. The use of a steady state is endorsed, as a continuous period of 24 hour indirect calorimetry measurements to determine REE or total energy expenditure (TEE) is not feasible (McClave, Spain, et al., 2003). Therefore, both researchers and practitioners rely on short duration (< 60 minutes) indirect calorimetry measurements from which a steady state can be determined. A steady state is a period of metabolic equilibrium where substrate metabolism at the cellular or tissue level represents that being measured at the respiratory or mouth level using indirect calorimetry (Brandi et al., 1997; McClave, Spain, et al., 2003). Accurate determination of a steady state period is essential to avoid respiratory artifacts and provide a true measure of REE (Compher et al., 2006; McClave & Snider, 1992). However, varying recommendations for steady state criteria are reported within the literature (Liusuwan, Palmieri, Kinoshita, & Greenhalgh, 2005;

McClave, Spain, et al., 2003; Schlein & Coulter, 2013; Shields et al., 2013; Wooley & Sax, 2003) and some authors do not report the steady state criterion used in their study, which contributes to the confusion (Garrel & de Jonge, 1993; Gottschlich et al., 1997; Hart et al., 2000; Peck et al., 2004; Tancheva et al., 2005; Wall-Alonso et al., 1999).

In 2003 McClave, Spain, et al., compared different steady state criteria and identified the most accurate as five consecutive averaged minutes during which oxygen consumption (VO_2) and carbon dioxide production (VCO_2) varied by $\leq 10\%$. This was also considered the most stringent criterion and McClave, Spain, et al. (2003) noted that as the stringency decreased so too did the correlation to 24 hour energy (**Table 31**). Reeves et al. (2004) extended this work by examining the accuracy of shorter steady state periods and found no significant difference between 5 and 4 minute criteria, and 5 and 3 minute criteria (**Table 31**). When examined using Bland-Altman plots to a predefined agreement level of $\pm 2\%$, it was identified that the 3 minute measure was unacceptable (-2.2 - 3.6%) while the 4 minute was within the acceptable agreement (-1.2 - 2.0%) (**Table 31**). However, the mean REE between the 5 and 3 minute steady states was relatively small (88 kJ/day) (McEvoy et al., 2009). Smallwood and Nilesch (2012) further demonstrated that there were no significant differences between a 5 minute steady state and 4 or 3 minutes, in a paediatric critical care population (**Table 31**). This was similarly observed in an adult traumatic brain injury (TBI) cohort by McEvoy et al. (2009) who found no significant differences between a steady state of 5 minutes and 4, 3 or 2 minutes (**Table 31**).

The work by these authors (McClave, Spain, et al., 2003; McEvoy et al., 2009; Reeves et al., 2004; Smallwood & Nilesch, 2012) has formed the basis of the steady state criteria algorithm for the current study (**Figure 7**). Subset analysis, exploring the different criteria used for steady state, was conducted with the two participants who achieved at least nine out of the ten

criteria. Overall, the maximal difference between the most stringent criterion and all others was < 116 kJ/day with a small spread of data, as indicated by the relatively small standard deviation (**Table 20**). Participant one demonstrated a pattern of increasing difference with diminishing stringency as observed by McClave, Spain, et al. (2003) and Reeves et al. (2004). However, this was not replicated by the other participant. Findings from these data cannot be conclusively drawn secondary to the small sample size restricting statistical analysis. However, based on these data the results suggest that less stringent steady state criteria were valid for non-ventilated moderate burn patients, which has implications for time and resources with routine indirect calorimetry measurements.

Ideally a steady state criterion should maximise the number of successful REE measurements while accurately determining 24 hour REE. A stringent steady state that excludes a large number of measurements is not feasible for research and clinical practice. McClave, Spain, et al. (2003) found that 73% of subjects achieved a steady state using the most stringent criteria. However, the study was undertaken on a cohort of sedated and ventilated patients where sedation is known to enhance the achievement of a steady state (Compher et al., 2006). This is likely to have resulted in a higher proportion achieving the stringent criteria compared to a population of non-sedated participants. Conversely, Smallwood and Niles (2012) found that only 56% of ventilated paediatric participants achieved the most stringent steady state criterion. In non-ventilated participants, Reeves et al. (2004) and McEvoy et al. (2009) have reported values for achievement of the strictest criterion ranging from 54 to 59% (**Table 31**). Evidence suggests that relaxation of the steady state criteria increases the rate of achievement without compromising the accurate determination of energy expenditure, as summarised in **Table 31** (McEvoy et al., 2009; Reeves et al., 2004; Smallwood & Niles, 2012). In the current study only two participants (33%) achieved the most stringent steady state criterion, while two achieved a steady state with a relaxed time period as described by Reeves et al. (2004). Two

participants failed to achieve a steady state and therefore the entire indirect calorimetry measurement was averaged to determine REE (**Table 19**). These rates of steady state achievement are lower than those cited in the literature, which have varied from 54 – 73% (**Table 31**) (McClave, Spain, et al., 2003; McEvoy et al., 2009; Reeves et al., 2004; Smallwood & Niles, 2012). Reasons for this may include poor ability of participants to adhere to the pre-test rest period, to remain awake and still during the test, and external disruptions which occurred during the measurement.

A rest period immediately prior to an indirect calorimetry measurement is recommended to avoid artificially elevated REE due to activity or movement. Rest period recommendations vary from 10 to 30 minutes with all stipulating that the individual does not talk or move during the time (Compher et al., 2006; Fullmer et al., 2015; Schlein & Coulter, 2013). A minimum rest period of 20 minutes was used in the current study. In accordance with the study protocol, the researcher entered the participant's room at approximately 0600 hours following the nursing round. Frequently participants used the bathroom, an estimated five meter walk from their bed, to void prior to the measurement. This is unlikely to have had a significant impact on their ability to achieve a rested state as Fredrix, Schoffelen, Ceulemans, and Saris (1990) found no significant difference in REE between subjects who slept overnight at the laboratory compared to those who slept at home, awoke, travelled by car and walked to the laboratory (NS); both completing a 30 minute rested period prior to the measurement.

Table 31

Summary of articles evaluating steady state criteria for indirect calorimetry measurements

Citation	Cohort characteristics	Steady state definition		Proportion of participants meeting the criteria (%)	Findings	Conclusions
		Criteria	Value (kJ/day)			
McClave, Spain, et al. (2003)	22 ventilated non-burn critically ill patients 13M 9F 52.8 years (16 – 84 yrs) (SD NR)	VO ₂ and VCO ₂ $\Delta \leq 10\%$ for 5 min (SS10)	8356	73	<ul style="list-style-type: none"> • 24 hour REE 8356 \pm 376 kJ/d • Correlation with 24 hour REE <ul style="list-style-type: none"> - SS10 r = 0.943 (NS) - SS15 r = 0.912 (NS) - SS20 r = 0.817 (NS) 	The most accurate SS criterion is 5 minutes VO ₂ and VCO ₂ $\Delta \leq 10\%$ for critically ill adults.
		VO ₂ and VCO ₂ $\Delta \leq 15\%$ for 5 min (SS15)	8180	95		
		VO ₂ and VCO ₂ $\Delta \leq 20\%$ for 5 min (SS20)	8193	86		
McEvoy et al. (2009)	20 spontaneously breathing traumatic brain injury patients 16M 4F 39.1 \pm 13.8 yrs (17 – 60 yrs)	VO ₂ and VCO ₂ CV $\leq 10\%$ and RQ $\leq 5\%$ for 5 min	6675	59	<ul style="list-style-type: none"> • mREE 6675 \pm 1485 kJ/d • 5 min SS compared to 4 min SS <ul style="list-style-type: none"> - p = 0.50^a - r = 0.99^b - Bias 4.2 kJ/day^c - Agreement $\pm 10\%$ is 100%^c • 5 min SS compared to 3 min SS <ul style="list-style-type: none"> - p = 0.35^a - r = 0.975^b - Bias 8.4 kJ/day^c - Agreement $\pm 10\%$ is 96%^c • 5 min SS compared to 2 min SS <ul style="list-style-type: none"> - p = 0.18^a - r = 0.949^b - Bias 62.7 kJ/day^c - Agreement $\pm 10\%$ is 88%^c 	A 4 minute and 3 minute steady state criteria are acceptable for adults with a traumatic brain injury.
		VO ₂ and VCO ₂ CV $\leq 10\%$ and RQ $\leq 5\%$ for 4 min	6759	70		
		VO ₂ and VCO ₂ CV $\leq 10\%$ and RQ $\leq 5\%$ for 3 min	6675	76		
		VO ₂ and VCO ₂ CV $\leq 10\%$ and RQ $\leq 5\%$ for 2 min	6700	84		

^a Wilcoxon signed ranks test used to determine statistical difference between the 5 minute criteria and alternative criteria

^b Spearman's correlations used to determine the strength of the relationship between the 5 minute criteria and alternative criteria

^c Bland-Altman test used to determine the agreement the 5 minute criteria and alternative criteria

^d Acceptable limit of agreement was $\pm 2\%$

Note. Δ = change; SS = steady state; NR = not reported; yrs = years; VO₂ = oxygen consumption (ml/min); VCO₂ = carbon dioxide produced (ml/min); RQ = respiratory quotient; REE = resting energy expenditure

Table 31 (continued)

Summary of articles evaluating steady state criteria for indirect calorimetry measurements

Citation	Cohort characteristics	Steady state definition		Proportion of participants meeting the criteria (%)	Findings	Conclusions		
		Criteria	Value (kJ/day)					
Reeves et al. (2004)	39 spontaneously breathing oncology (n = 22) and healthy (n = 17) participants 16M and 5F 61 ± 21 yrs (range NR)	VO ₂ , VCO ₂ and RQ Δ ≤ 10% for 5 min	6379	54	<ul style="list-style-type: none"> • mREE 6675 ± 1271 kJ/day • 5 min SS compared to 4 min SS <ul style="list-style-type: none"> - p = 0.52^a - r = 0.99^b - Bias -5.4 kJ/day^c - Limit of agreement range -1.2 – 2%^d • 5 min SS compared to 3 min SS <ul style="list-style-type: none"> - p = 0.60^a - r = 0.98^b - Bias 0.4 kJ/day^c - Limit of agreement range -2.2 – 3.4%^d 	A 4 minute steady state criterion is acceptable for adult oncology and healthy participants.		
		VO ₂ , VCO ₂ and RQ Δ ≤ 10% for 4 min	6308	69				
		VO ₂ , VCO ₂ and RQ Δ ≤ 10% for 3 min	6291	97				
Smallwood and Niles (2012)	34 ventilated critically ill non-burn paediatric patients 12M 22F 4.37 ± 5.10 yrs (range NR)	VO ₂ and VCO ₂ Δ ≤ 10% for 5 min	2107	56			<ul style="list-style-type: none"> • 5 min SS compared to 4 min SS <ul style="list-style-type: none"> - p = NS^a - r = 0.996^b - Bias 11.7 kJ/day^c - Agreement ± 10% is 96%^c • 5 min SS compared to 3 min SS <ul style="list-style-type: none"> - p = NS^a - r = 0.990^b - Bias 24.2 kJ/day^c - Agreement ± 10% is 88%^c 	A 4 minute and 3 minute steady state criteria are acceptable for critically ill ventilated children.
		VO ₂ and VCO ₂ Δ ≤ 10% for 4 min	2102	69				
		VO ₂ and VCO ₂ Δ ≤ 10% for 3 min	2115	93				

^a Wilcoxon signed ranks test used to determine statistical difference between the 5 minute criteria and alternative criteria

^b Spearman's correlations used to determine the strength of the relationship between the 5 minute criteria and alternative criteria

^c Bland-Altman test used to determine the agreement the 5 minute criteria and alternative criteria

^d Acceptable limit of agreement was ± 2%

Note. Δ = change; SS = steady state; NR = not reported; yrs = years; VO₂ = oxygen consumption (ml/min); VCO₂ = carbon dioxide produced (ml/min); RQ = respiratory quotient; REE = resting energy expenditure

A 20 minute rest period for the current study enabled the indirect calorimetry measurement to fit into scheduled ward activities such as the medical team round which occurred at 0700 hours. The researcher also completed calibration of the indirect calorimeter in the room during the rest period to ensure consistent environmental conditions. However, the ability of participants to adhere to the 20 minute period of complete rest is questionable as despite the researcher's request that the participants were not to move or speak during this period, some were unable to remain still. For example, one participant turned on their television during the period and another asked when the test would begin. Another limitation may have been the calibration of the indirect calorimeter in the participant's room during the rest period. The protocol was designed to ensure that the calibration environment conditions matched the test conditions. An early trial of the study protocol indicated that calibration in a different room (the ward gym where the Ultima CPX was stored), which had environmental conditions different to those of the participant's room, resulted in inaccurate and unreliable indirect calorimetry measurements. Furthermore, it was determined impractical to calibrate the equipment before a rest period as this would have involved entering and waking the participants at 0530 hours. Therefore, the protocol was designed to combine the calibration with the rest period. While noise was kept to a minimum by the researcher during calibration there is the possibility that it affected the participant's ability to achieve a true rested state. As such, poor adherence to the resting period by participants may have resulted in an elevated REE and contributed to low achievement of the primary steady state criterion.

The difficulty of some participants to remain awake during the indirect calorimetry measurement may also have contributed to the low achievement of a steady state. The researcher noted that participants who oscillated between asleep and awake, often with startled awakenings, had a high degree of observed variability in minute REE, VO_2 and VCO_2 data (**Figure 10**). The metabolic rate has been observed to decrease during sleep by between 5 and

25% (Shapiro & Flanigan, 1993). However, evidence is lacking as to the impact of a cycling pattern of awake and light sleep on the achievement of a steady state. Gottschlich et al. (1997) found no significant difference between REE when awake (10571 ± 1655 kJ) and asleep (9864 ± 12166 kJ) in a paediatric burn population. Conversely, Royall et al. (1994) found a difference between night and day REE in ventilated adult burn patients ($p < 0.005$). The difference between the two studies may be attributed to the criteria used to define sleep with Gottschlich et al. (1997) applying a more stringent measure than Royall et al. (1994). Another overlooked factor may have been the difference in the TBSA, as the Gottschlich et al. (1997) cohort had a higher mean TBSA at $55.78 \pm 17.5\%$ (20 – 82%) than Royall et al. (1994) at $36.7 \pm 4.2\%$ (no range reported). Potentially the maximal metabolic rate was reached in the Gottschlich et al. (1997) cohort which negated the drop in energy expenditure observed during sleep. The differing findings from these authors make interpretation of the current study challenging. Potentially those participants who fell asleep during the measurement had a lower REE. However, this may have been counteracted by the impact of a startled awakening and the associated increase in REE. Participants who oscillated between awake and asleep may have had a lower rate of steady state achievement.

Conditions during an indirect calorimetry test should be quiet and those being measured should remain still, or have minimal movement, to ensure that a steady state is achieved but also that true resting conditions are measured (Fullmer et al., 2015). Levine, Schleusner, and Jensen (2000) demonstrated that fidgeting (e.g., hand and foot tapping, moving arms) resulted in an increased energy expenditure compared to true rested conditions ($p < 0.001$). Movement or agitation has been reported to reduce the likelihood of steady state achievement (Fullmer et al., 2015). Frankenfield, Sarson, Blosser, Cooney, and Smith (1996) observed critical care patients who successfully completed an indirect calorimetry measurement had a higher level of sedation compared to those who failed to complete the tests. In the current study, the researcher observed

fidgeting or movement during each measurement ranging from slight hand and feet movement or twitches, scratching, adjustment of the face tent through to having a drink of water and speaking to the researcher. The majority of participants remained relaxed during the measurement however, obvious agitation was observed in participant one to the extent that the measurement was ceased early. During one test a participant's phone rang causing an interruption and in another the orderly knocked and entered the room; this was avoided in later tests by placing a "Do Not Disturb" sign on the participant's door. In summary, adherence to minimal movement in a quiet environment proved challenging and may have contributed to the low achievement of a steady state and could potentially result in an elevated REE.

5.1.2 Accuracy of the Ultima CPX system

The Ultima CPX has been used by previous researchers for a range of medical conditions including burn injuries, cancer and liver disease (Peck et al., 2004; Pimenta et al., 2014). However, studies comparing different models of indirect calorimeters have identified inaccuracies with the Ultima systems (CPX and the CCM version) which may account for challenges experienced in the current study. Cooper et al. (2009) compared the Ultima CPX and four other indirect calorimeters (MedGem, TrueOne 2400, Vmax Encore 29 System and the Korr ReeVue) to the "gold standard", but no longer in production, Deltatrac II. The REE and respiratory quotient (RQ), reported as respiratory exchange rate (RER), for the Ultima CPX was significantly different from the Deltatrac II ($p < 0.05$). The within-subject reliability for the Ultima CPX, measured by comparing the co-efficient of variation for the Ultima to that of the Deltratrac II, was found to be significantly higher for REE ($p < 0.01$) but not for RER. The authors concluded that overall none of the systems, including the Ultima CPX, were valid and reliable for research purposes when compared to the Deltatrac II. In a recent publication, Graf et al (2015) compared three indirect calorimeters, the Ultima CCM, which has the same

software and hardware as the CPX (N. Romeo, personal communication, October 13, 2015), the Deltatrak II and the Quark RMR, by simultaneously connecting them to a ventilated patient. The Ultima CCM was significantly different to the Deltatrak II for VO_2 , carbon dioxide production VCO_2 , RQ and REE (all $p < 0.001$). REE determined by the Ultima CCM was 17% higher than the Deltatrak II ($p < 0.05$). However, this was not a systematic error leading the authors to conclude that the CCM is inaccurate for critically ill ventilated patients. The authors concluded that the initial development of the Ultima CCM for use with healthy exercising subjects may compromise its effectiveness in critically ill ventilated populations. These findings question the accuracy of the Ultima CPX system and may have contributed to the variability of results in the current study.

5.1.3 Accuracy of the Ultima CPX face tent

The RQ is the ratio of VCO_2 to VO_2 and reflects metabolic gas exchange, or energy substrate utilisation, at the cellular level. As cellular metabolism cannot be directly measured, we measure the ratio of VCO_2 to VO_2 through expired gas at the mouth (or lung), referred to as the RER. The assumption is that during rest the RER equals the RQ therefore providing a measure of cellular gas exchange (Manore, Meyer, & Thompson, 2009). During hyperventilation or exercise, acid-base balance is disrupted resulting in higher VCO_2 levels, which will increase the RER (i.e., the gas exchange at the lung or mouth level). Therefore, the assumption that RER equals RQ may not hold true. The general nutrition literature refers to RQ rather than RER as indirect calorimetry is conducted in a rested state, therefore there is an assumption that RQ equals RER. RQ has been purported to indicate energy substrate utilisation and is used more accurately as a method to validate indirect calorimetry tests (McClave, Lowen, et al., 2003).

The accepted physiological range of RQ is 0.67 to 1.3 (McClave, Lowen, et al., 2003). Historically, RQ has been purported as a marker for energy substrate utilisation with fat corresponding to an RQ of 0.7, protein 0.8 and carbohydrate 1.0 (McClave, Lowen, et al., 2003). However, a study by McClave, Lowen, et al. (2003) concluded that the RQ was unreliable and of little value in the indication of macronutrient metabolism. Theoretically, an RQ value > 1.0 can be considered an indicator for overfeeding and < 0.85 an indicator of underfeeding. However, McClave, Lowen, et al. (2003) reported that the RQ value had low sensitivity for under- and overfeeding at 55.8% and 38.5%, respectively. These results were replicated by Liusuwan, Palmieri, and Greenhalgh (2008) in a paediatric burn injury cohort who reported that RQ had poor sensitivity and specificity for under- and overfeeding. The authors concluded that the interpretation of RQ during disease states was challenging and could be influenced by errors in the indirect calorimetry system such as leaks and calibration errors, hyper- and hypoventilation of the patient, and derangements in the patients substrate metabolism (e.g., glucose with diabetes mellitus) (Liusuwan et al., 2008; McClave, Lowen, et al., 2003). The most appropriate use for the RQ is to validate indirect calorimetry tests (McClave, Lowen, et al., 2003; Schlein & Coulter, 2013).

A review by Compher et al. (2006) concluded that the RQ range used to validate indirect calorimetry measurement was 0.7 to 1.0. Values outside this range warrant investigation as they are likely to indicate errors. The mean RQ of the current study was 1.08 ± 0.14 (0.91 – 1.31), which is above the validation range but within the physiological range (**Table 21**). Within the current cohort, five measurements (83%) had an RQ value above the validation range and of those, three measurements were marginally above the validation range (1.01, 1.05 and 1.06) and one had an RQ value above the physiological range (1.31). The proportion of elevated values is larger than that observed in other studies of 11.4 to 24% for individuals with burn injuries (Liusuwan et al., 2008; Saffle et al., 1990) and 3.1% for medical and surgical

patients (McClave, Lowen, et al., 2003). A possible reason for the elevated RQ in the current study is overfeeding. However, RQ is not considered a valid indicator for overfeeding (McClave, Lowen, et al. (2003) and Liusuwan et al. (2008) and estimated energy intake of the current study cohort did not indicate overfeeding of participants. Specifically, three out of the five participants with RQ values > 1.0 were estimated to have an energy intake less than their requirements (21 - 30% deficit) and two had energy intake above their estimated requirements (14 - 54%). Hyperventilation is an alternative and more likely cause for the elevated RQ values.

Discomfort, pain and agitation may cause acute hyperventilation (Feurer & Mullen, 1986). During acute hyperventilation the VCO_2 production at the lung level, or the RER, becomes elevated in order to correct for the increased oxygen intake associated with the rapid and shallow breathing. As we assume that the RER equates to the RQ during rest, this is interpreted as an elevated RQ value and may mistakenly be interpreted as changes in energy substrate utilisation. As previously discussed, agitation was observed during measurements of indirect calorimetry within this cohort. In particular, the indirect calorimetry test with an RQ value of 1.31 was observed by the researcher as having the most agitated participant indicated by the need to cease the measurement prematurely. Closer analysis of the VCO_2 values indicated that the three highest RQ values (1.31, 1.15 and 1.06) were associated with VCO_2 values above the physiological range, thus providing support for the presence of hyperventilation.

Other possible explanations for the elevated RQ value include calibration error and a leak in the system (McClave, Lowen, et al., 2003). It is possible that there may have been an error within the calibration of the indirect calorimeter system as five out of six measurements had an elevated RQ which warrants further investigation. Another potential source of error is the open face tent collection system. The face tent equipment requires the adjustment of the fan speed to maximise the CO_2 readings (**Figure 6**). However, the researcher and colleagues observed

that this system lacked precision despite additional consultation and testing with the Ultima CPX Australian distributor. If the fan speed was set too fast this would cause additional room air to be drawn into the system, which would reduce the VCO_2 and therefore the RQ; however, if the fan speed was too slow then inadequate room air would have been drawn into the system which would elevate VCO_2 . This effect may have been compounded by the use of a bacterial filter. Pilot testing was conducted in consultation with the Ultima CPX Australian distributor in the Edith Cowan University (ECU) laboratory investigating the bacterial filter and found no marked difference once software settings were correctly adjusted to account for the specified dead space of the filter. However, it is possible that due to the imprecise nature of the fan speed settings the filter did affect the flow of air.

To investigate the accuracy of the face tent the researcher initiated a concurrent but separate study in the ECU laboratory comparing the face tent collection system with two alternative systems, the face mask and the mouthpiece with nose clip. All tests were conducted using the Ultima CPX equipment (Medgraphics, USA) and the same standardised protocol, with ethics approval from the Edith Cowan University HREC (ECU 12622). Twelve healthy adult participants (7 female and 5 males) with a mean \pm SD age of 27 ± 10 years and body mass index (BMI) 23.9 ± 3.6 kg/m² completed concurrent 20 minute measurements for each collection system (60 minutes per day) on three separate occasions. The mean \pm SD for the RQ was 0.92 ± 0.21 , 0.82 ± 0.06 and 0.84 ± 0.07 , for the face tent, face mask and mouthpiece, respectively. There was no significant difference between the mean combined RQ for all three systems ($p = 0.125$). However, the relatively wide variation between the face tent and the other two systems in occasions two and three, as evidenced by the large standard deviations in **Figure 13**, indicate poor repeatability of the face tent.

In summary, the elevated RQ observed with the face tent in the current study is likely due to physiological and system errors and may have affected the accuracy of the observed REE measurement. Hyperventilation likely occurred within the cohort secondary to the pain and discomfort associated with burn injuries and the inability of some participants to achieve rested conditions before and during the test. Unidentified system errors may have also been present in the face tent setup process, warranting further investigation.

5.1.4 Participant recruitment

It was anticipated that participant recruitment would commence in November 2014 and cease mid-March 2015, a 19 week period. However, due to unanticipated delays in servicing of the Ultima CPX and meeting the hospital infection control requirements and the move of the Western Australian (WA) State Adult Burn Unit from Royal Perth Hospital (RPH) to the newly opened Fiona Stanley Hospital (FSH), the recruitment period was delayed and shortened from 19 weeks to 17 weeks. The higher than expected exclusion rate due to facial burn injuries inhibiting the use of the face tent, and lower than expected admission rate of suitable patients based on previous admissions to RPH, contributed to the lower than expected recruitment of participants.

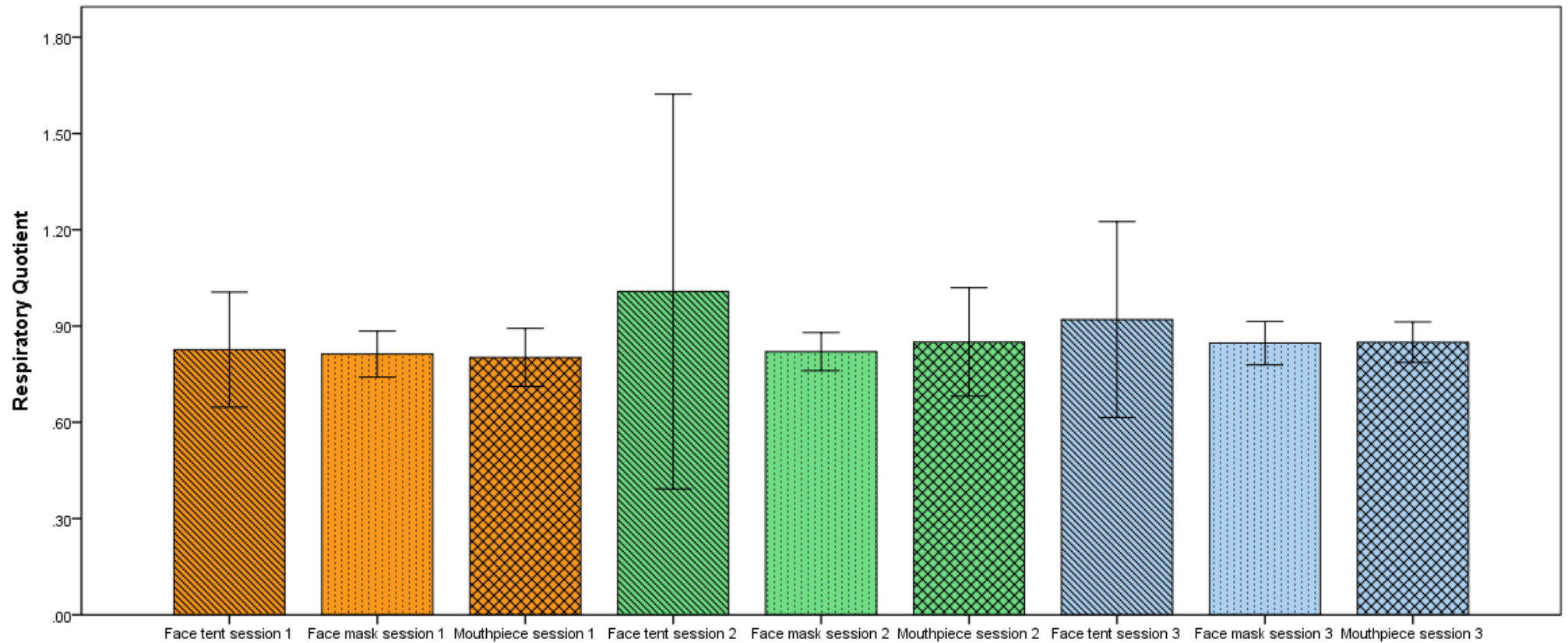


Figure 13. Mean respiratory quotient values and standard deviation error bars for three different collection systems (face tent, face mask and mouthpiece) on three test occasions in twelve healthy participants indicating no difference between collection systems for combined RQ values ($p = 0.125$).

Note. Respiratory quotient is calculated as ratio of oxygen consumption (VO_2) to carbon dioxide production (VCO_2)

Prior to the study commencing it was identified that the Ultima CPX would require servicing and replacement of parts to ensure the accuracy of measurements. Despite the researcher's best efforts, there were unexpected delays in the servicing of the Ultima CPX and the equipment did not return to ECU until the 30th of October 2014. Due to the frequent use of indirect calorimeters with hospitalised patients, including burn injuries, it was not anticipated that there would be a delay in the approval for use of the Ultima CPX by hospital infection control. However, infection control expressed concerns regarding the risk of transference of bacteria and the inability to adequately sterilise the equipment. Following this meeting the researcher liaised with the Australian distributor who suggested and provided several bacterial filters. In a second meeting with infection control staff on the 26th of November 2014 the Bird Healthcare bacterial filter was approved for use.

Admission rates for the RPH Burn Unit in 2013 indicated that one to two patients meeting the total body surface area (TBSA) burn injury inclusion criteria were admitted each week to the unit. During the recruitment period for the current study 27 patients meeting the inclusion criteria were identified. However, nine were excluded due to the presence of facial injury negating the use of the face tent, three were unable to provide informed consent and four declined to participate.

5.1.5 Change to the timing and frequency of indirect calorimetry measurements

In discussions with clinicians in the burn team, the initial indirect calorimetry measurement was to be conducted within 72 hours of admission to the burn unit in the proposed study design. Despite the researchers attempts to conduct initial measurements within this period it became apparent that this was not feasible. Although patients were identified on admission there was often a delay in the burn unit dietitian speaking with them, as they were occupied with other

health professionals due to the acuity of their injuries; and participants were often required to have surgery which either meant a delay in the FSH dietitian speaking with them or that the researcher was required to wait 48 hours to conduct the measurement. Given the pilot nature of the study it was decided that conducting the indirect calorimetry measurement, irrespective of the time post-injury, was the priority. Therefore, initial measurements occurred as soon as possible and the number of days post-admission was documented by the researcher for later consideration.

In discussion with the site medical team, it was planned that each participant would have three indirect calorimetry measurements completed with two occurring during admission and one as an outpatient. However, the majority of participants were discharged from hospital before the second indirect calorimetry measurement could be completed and some participants required surgical intervention for their injuries, which restricted the ability to conduct subsequent inpatient measurements. The proposed study design included an outpatient indirect calorimetry measurement six weeks following hospital discharge. However, as data collection was delayed several months the researcher had limited time available to collect these data and the decision was made to prioritise the inpatient measurements.

5.2 Recommendations

Recommendations for both research and clinical practice are provided based on findings from the present study with consideration to the literature, as well as the limitations and challenges encountered in the project execution. Additional research is required to further define the REE of individuals with a moderate burn injury using a larger sample size ($n = 30$) that includes participants representing a broad range of age, gender and body composition to determine the influence of such variables on energy expenditure. Further analysis of the Ultima CPX system

is required to understand the aetiology of observed errors and confirm the accuracy of the face tent system. This could be achieved by simultaneously connecting the Ultima CPX to other indirect calorimetry systems (Graf et al., 2015). Given the observed inaccuracies and challenges encountered with the use of the Ultima CPX, and large time demands required to operate the system, it is recommended that consideration be given to the use of validated user-friendly indirect calorimetry systems such as the COSMED Quark RMR or Fitmate Pro. Such systems provide a canopy hood collection system which would enable the recruitment of individuals with facial burn injuries. Further research should consider a steady state suitable for indirect calorimetry measurements with non-ventilated burn patients. Results of the current study suggest that a less stringent steady state criterion may provide accurate REE measurements and increase the proportion of successful tests however, this is based on a small sample and additional research is required to confirm these findings. Use of a relaxed yet accurate steady state criterion would have time and financial benefits for practitioners.

The protocol for indirect calorimetry measurements should be reviewed and examined for future research in moderate burn injuries and also the routine clinical use within the FSH burn unit. This should include consideration for an appropriate rest period; how best to obtain awake but rested conditions for participants during the measurement; the impact of pain, agitation and fidgeting on REE; and how to schedule measurements to avoid interruptions by other staff in a busy hospital environment. The impact of these indirect calorimetry protocol factors should be evaluated for clinical relevance and balanced with the benefits of accurately determining REE in burn patients. A 1045 kJ/day margin of error is acceptable for clinical use and is unlikely to result in significant weight change (Hasson et al., 2011). Therefore, further research is required to define a practical indirect calorimetry protocol which provides accurate and clinically relevant REE measurements for moderate burn injuries.

Further research on the TEE for individuals with a moderate burn injury utilising gold standard methodology such as double labelled water is warranted. The current study provided an indicative picture of total energy balance based on 24 hour dietary recall and estimated physical activity levels. However, more accurate methodology are required to determine TEE and the possible impact over time of under and over nutrition in patients with moderate burn injuries.

5.3 Conclusion

The aim of this observational pilot study was to describe and explore the REE of moderate burn injuries measured using indirect calorimetry and predicted using statistically derived mathematical equations; and understand the experience of participants undertaking an indirect calorimetry measurement. This study is novel in its exploration of moderate burn injuries as the majority of the literature has focused on the energy expenditure of major burn injuries. Moderate burn injuries represent the majority of burn-related hospital admissions within Australia and yet their energy expenditure remained undefined within the literature. The hypotheses were drawn from the observation of previous studies that moderate burn injuries would have a lower REE than major burn injuries and that the predictive methods for the determination of REE would be inaccurate. Given the numerous publications for the use of indirect calorimetry with non-ventilated hospitalised patients it was hypothesised that the indirect calorimetry measurements would be acceptable for study participants. Quantitative analysis was employed to evaluate each hypothesis in a cohort of five male and three female participants with moderate burn injuries.

Analysis revealed that individuals with a moderate burn injury experienced a lower REE than individuals with a major burn injury, a finding consistent with previous publications. Due to a small sample size the impact of potential confounding variables such as age, gender, body

composition and total body surface area (TBSA) could not be analysed. However, trends within the data, supported by previous publications, suggested that increasing age was inversely correlated with REE. Further research exploring the impact of such variables over the time course of the burn injury and subsequent recovery is warranted. Body composition in particular has been shown as a significant variable for REE in healthy individuals but remains unexplored for burn injuries. Based on the findings of this study it is recommended that the Schofield equation with a 5 to 10% injury factor is used with caution for the prediction of REE for moderate burn injuries when indirect calorimetry is not available. This study found that the indirect calorimetry procedure was acceptable to patients thus contributing to the body of literature advocating for routine application in burn centres.

To the researcher's knowledge, this study is the first to undertake an examination of energy expenditure exclusively in moderate burn injuries. It has shown the lower REE experienced by moderate burn injuries compared to major burn injuries, and that indirect calorimetry measurement is acceptable to patients, thus providing evidence to support the use of indirect calorimetry for routine best practice assessment for individuals with a burn injury. Future areas for research include repeating the study to gain a larger sample size, investigation and consideration to an alternative indirect calorimetry system to address measurement issues encountered in the current study and exploration of changes in energy expenditure over time for moderate burn injuries.

Chapter 6: References

6.1 References

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Appendix A: Ultima TGA registration

Public Summary

Summary for ARTG Entry: 149230 MGC Diagnostics Australia - Stress exercise monitoring system, pulmonary

ARTG entry for Medical Device Included Class IIa
Sponsor MGC Diagnostics Australia
Postal Address 28 Waverley Park Drive, MULGRAVE, VIC, 3170
 Australia
ARTG Start Date 15/01/2008
Product category Medical Device Class IIa
Status Active
Approval area Medical Devices

Conditions

The automatic conditions applicable to the inclusion of all kinds of medical devices in the Register are as specified in section 41FN of the Therapeutic Goods Act 1989.,

The standard conditions that are imposed under section 41FO of the Therapeutic Goods Act 1989 when kinds of medical devices are included in the Register are as set out in the following paragraphs.,

For a medical device included in the Register under Chapter 4 and imported into Australia, the Sponsor must ensure that information about the Sponsor is provided in such a way as to allow the sponsor to be identified.,

Each sponsor shall retain records of the distribution of all of the sponsor's medical devices included in the Register under Chapter 4. In the case of records relating to a Class AIMD medical device, Class III medical device, or Class IIb medical device that is an implantable medical device, the distribution records shall be retained for a minimum period of 10 years. In the case of records relating to any other device, the distribution records shall be retained for a minimum period of 5 years.,

The sponsor of a medical device included in the Register under Chapter 4 shall keep an up to date log of information of the kind specified in Regulation 5.8.,

It is a condition of inclusion in the ARTG that the sponsor of a medical device that is an AIMD, Class III or implantable Class IIb provides three consecutive annual reports to the Head of the Office of Product Review, Therapeutic Goods Administration following inclusion of the device in the ARTG (as specified in 5.8 of the regulations). Annual reports are due on 1 October each year. Reports should be for the period 1 July to 30 June. The first report following the date of inclusion in the ARTG must be for a period of at least six months but no longer than 18 months. Subsequent reports are to be provided on 1 October for a further 2 years. The annual report must include all complaints and adverse events received by the manufacturer relating to problems with the use of the device that have been received by them over the year. For orthopaedic implant prosthesis that have been re-classified from Class IIb to Class III medical devices, annual report information must be submitted if the device meets either of the following criteria: I. The device was subject to a TGA application audit based on revision rate when the device transitioned from Class IIb to Class III; and/or II. No devices were supplied to the Australian marketplace before 30 June 2012. As per the standard automatic condition, annual reports should be submitted each year for the first three years of inclusion as a Class III medical device on the ARTG.,

Where a medical device included in the Register, contains a substance which is included in the Fourth Schedule to the Customs (Prohibited Imports) Regulations or the Eighth Schedule to the Customs (Prohibited Exports) Regulations the Sponsor shall, at the time of importation or exportation of the medical device, be in possession of a licence and a permission for importation or exportation of each consignment of the goods as required by those regulations.,

A sponsor shall ensure that a medical device within their control is stored and transported in accordance with the instructions and information provided by the manufacturer.

Manufacturers

Name	Address
Medical Graphics Corp	350 Oak Grove Parkway ST PAUL, MN, 55127 United States Of America

Products

1. Stress exercise monitoring system, pulmonary			
Product Type	Medical device system	Effective date	15/01/2008
GMDN	36146 Stress exercise monitoring system, pulmonary		
Intended purpose	Stress Exercise system to uses analysers to measure parameters of pulmonary function during exercise.		

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Appendix B: Participant indirect calorimetry acceptability questionnaire



Project Title Pilot study: determination and analysis of resting energy expenditure using indirect calorimetry of individuals with

Principal Investigator Janica Bell

Contact 0408 751 312

Associate Investigator(s) Dr. F Wood, Dr D Edgar, Dr A. Stewart, A/Prof P. Lyons-Wall

Patient survey

Date Calorimetry performed _____

Please take 10 minutes to tell us about your experience undertaking metabolic testing using indirect calorimetry.

1. The amount of time taken to complete the metabolic testing was acceptable

Strongly disagree	Disagree	Neutral	Agree	Strongly agree
5	4	3	2	1

If you disagree, please explain reasons why:

2. The time of the morning the metabolic testing was undertaken was convenient to me

Strongly disagree	Disagree	Neutral	Agree	Strongly agree
5	4	3	2	1

If you disagree, please explain reasons why:

3. The following statements relate to your experience during the metabolic testing procedure.

		Please circle		
i	I felt comfortable during the procedure	Yes	No	If no, please provide further details:
ii	The room temperature was acceptable	Yes	No	If no, please provide further details:
iii	I was able to breathe normally with the face mask	Yes	No	If no, please provide further details:
iv	I was able to remain still during the procedure	Yes	No	If no, please provide further details:
v	I was able to relax during the procedure	Yes	No	If no, please provide further details:
vi	I felt pain during the procedure	Yes	No	If yes, please provide further details:
vii	I felt the urge to empty my <i>bladder</i> during the procedure	Yes	No	If yes, please provide further details:
viii	I felt the urge to open my <i>bowels</i> during the procedure	Yes	No	If yes, please provide further details:

4. I felt there was adequate privacy where the metabolic testing was undertaken (circle one)

Strongly disagree	Disagree	Neutral	Agree	Strongly agree
5	4	3	2	1

If you disagree with the previous statement, how do you feel privacy could be improved?

5. I would be willing to have the metabolic testing procedure repeated in the future (circle one)

Strongly disagree	Disagree	Neutral	Agree	Strongly agree
5	4	3	2	1

6. I feel it would be acceptable for patients with a burn injury to have metabolic testing measurements performed as part of their routine care (circle one)

Strongly disagree	Disagree	Neutral	Agree	Strongly agree
5	4	3	2	1

7. From your experience, is there anything you can think of that would have made the metabolic testing procedure a better experience for you?

Any further comments?

Thank you for your assistance

This survey has been used with permission from H. Mayr and A. Nevin from Princess Alexandra Hospital.

Scored Patient-Generated Subjective Global Assessment (PG-SGA)

Patient ID Information

History (Boxes 1-4 are designed to be completed by the patient.)

1. Weight (See Worksheet 1)

In summary of my current and recent weight:

I currently weigh about _____ pounds

I am about _____ feet _____ tall

One month ago I weighed about _____ pounds

Six months ago I weighed about _____ pounds

During the past two weeks my weight has:

decreased ⁽¹⁾ not changed ⁽⁰⁾ increased ⁽⁰⁾

Box 1

2. Food Intake: As compared to my normal intake, I would rate my food intake during the past month as:

- unchanged ⁽⁰⁾
- more than usual ⁽⁰⁾
- less than usual ⁽¹⁾

I am now taking:

- normal food but less than normal amount ⁽¹⁾
- little solid food ⁽²⁾
- only liquids ⁽³⁾
- only nutritional supplements ⁽³⁾
- very little of anything ⁽⁴⁾
- only tube feedings or only nutrition by vein ⁽⁰⁾

Box 2

3. Symptoms: I have had the following problems that have kept me from eating enough during the past two weeks (check all that apply):

- no problems eating ⁽⁰⁾
- no appetite, just did not feel like eating ⁽³⁾
- nausea ⁽¹⁾
- vomiting ⁽³⁾
- constipation ⁽¹⁾
- diarrhea ⁽³⁾
- mouth sores ⁽²⁾
- dry mouth ⁽¹⁾
- things taste funny or have no taste ⁽¹⁾
- smells bother me ⁽¹⁾
- problems swallowing ⁽²⁾
- feel full quickly ⁽¹⁾
- pain; where? ⁽³⁾ _____
- other** ⁽¹⁾ _____

** Examples: depression, money, or dental problems

Box 3

4. Activities and Function: Over the past month, I would generally rate my activity as:

- normal with no limitations ⁽⁰⁾
- not my normal self, but able to be up and about with fairly normal activities ⁽¹⁾
- not feeling up to most things, but in bed or chair less than half the day ⁽²⁾
- able to do little activity and spend most of the day in bed or chair ⁽³⁾
- pretty much bedridden, rarely out of bed ⁽³⁾

Box 4

Additive Score of the Boxes 1-4 A

The remainder of this form will be completed by your doctor, nurse, or therapist. Thank you.

5. Disease and its relation to nutritional requirements (See Worksheet 2)

All relevant diagnoses (specify) _____

Primary disease stage (circle if known or appropriate) I II III IV Other _____

Age _____

Numerical score from Worksheet 2 B

6. Metabolic Demand (See Worksheet 3)

Numerical score from Worksheet 3 C

7. Physical (See Worksheet 4)

Numerical score from Worksheet 4 D

Global Assessment (See Worksheet 5)

- Well-nourished or anabolic (SGA-A)
- Moderate or suspected malnutrition (SGA-B)
- Severely malnourished (SGA-C)

Total PG-SGA score

(Total numerical score of A+B+C+D above)
(See triage recommendations below)

Clinician Signature _____ RD RN PA MD DO Other _____ Date _____

Nutritional Triage Recommendations: Additive score is used to define specific nutritional interventions including patient & family education, symptom management including pharmacologic intervention, and appropriate nutrient intervention (food, nutritional supplements, enteral, or parenteral triage). First line nutrition intervention includes optimal symptom management.

- 0-1 No intervention required at this time. Re-assessment on routine and regular basis during treatment.
- 2-3 Patient & family education by dietitian, nurse, or other clinician with pharmacologic intervention as indicated by symptom survey (Box 3) and laboratory values as appropriate.
- 4-8 Requires intervention by dietitian, in conjunction with nurse or physician as indicated by symptoms survey (Box 3).
- ≥ 9 Indicates a critical need for improved symptom management and/or nutrient intervention options.

Worksheets for PG-SGA Scoring

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Boxes 1-4 of the PG-SGA are designed to be completed by the patient. The PG-SGA numerical score is determined using 1) the parenthetical points noted in boxes 1-4 and 2) the worksheets below for items not marked with parenthetical points. Scores for boxes 1 and 3 are additive within each box and scores for boxes 2 and 4 are based on the highest scored item checked off by the patient.

Worksheet 1 - Scoring Weight (Wt) Loss

To determine score, use 1 month weight data if available. Use 6 month data only if there is no 1 month weight data. Use points below to score weight change and add one extra point if patient has lost weight during the past 2 weeks. Enter total point score in Box 1 of the PG-SGA.

Wt loss in 1 month	Points	Wt loss in 6 months
10% or greater	4	20% or greater
5-9.9%	3	10 -19.9%
3-4.9%	2	6 - 9.9%
2-2.9%	1	2 - 5.9%
0-1.9%	0	0 - 1.9%

Score for Worksheet 1 =
Record in Box 1

Worksheet 2 - Scoring Criteria for Condition

Score is derived by adding 1 point for each of the conditions listed below that pertain to the patient.

Category	Points
Cancer	1
AIDS	1
Pulmonary or cardiac cachexia	1
Presence of decubitus, open wound, or fistula	1
Presence of trauma	1
Age greater than 65 years	1

Score for Worksheet 2 =
Record in Box B

Worksheet 3 - Scoring Metabolic Stress

Score for metabolic stress is determined by a number of variables known to increase protein & calorie needs. The score is additive so that a patient who has a fever of > 102 degrees (3 points) and is on 10 mg of prednisone chronically (2 points) would have an additive score for this section of 5 points.

Stress	none (0)	low (1)	moderate (2)	high (3)
Fever	no fever	>99 and <101	≥101 and <102	≥102
Fever duration	no fever	<72 hrs	72 hrs	> 72 hrs
Steroids	no steroids	low dose (<10mg prednisone equivalents/day)	moderate dose (≥10 and <30mg prednisone equivalents/day)	high dose steroids (≥30mg prednisone equivalents/day)

Score for Worksheet 3 =
Record in Box C

Worksheet 4 - Physical Examination

Physical exam includes a subjective evaluation of 3 aspects of body composition: fat, muscle, & fluid status. Since this is subjective, each aspect of the exam is rated for degree of deficit. Muscle deficit impacts point score more than fat deficit. Definition of categories: 0 = no deficit, 1+ = mild deficit, 2+ = moderate deficit, 3+ = severe deficit. Rating of deficit in these categories are *not* additive but are used to clinically assess the degree of deficit (or presence of excess fluid).

Fat Stores:

	0	1+	2+	3+
orbital fat pads	0	1+	2+	3+
triceps skin fold	0	1+	2+	3+
fat overlying lower ribs	0	1+	2+	3+
Global fat deficit rating	0	1+	2+	3+

Muscle Status:

	0	1+	2+	3+
temples (temporalis muscle)	0	1+	2+	3+
clavicles (pectoralis & deltoids)	0	1+	2+	3+
shoulders (deltoids)	0	1+	2+	3+
interosseous muscles	0	1+	2+	3+
scapula (latissimus dorsi, trapezius, deltoids)	0	1+	2+	3+
thigh (quadriceps)	0	1+	2+	3+
calf (gastrocnemius)	0	1+	2+	3+
Global muscle status rating	0	1+	2+	3+

Fluid Status:

	0	1+	2+	3+
ankle edema	0	1+	2+	3+
sacral edema	0	1+	2+	3+
ascites	0	1+	2+	3+
Global fluid status rating	0	1+	2+	3+

Point score for the physical exam is determined by the overall subjective rating of total body deficit.

No deficit	score = 0 points
Mild deficit	score = 1 point
Moderate deficit	score = 2 points
Severe deficit	score = 3 points

Score for Worksheet 4 =
Record in Box D

Worksheet 5 - PG-SGA Global Assessment Categories

Category	Stage A Well-nourished	Stage B Moderately malnourished or suspected malnutrition	Stage C Severely malnourished
Weight	No wt loss OR Recent non-fluid wt gain	~5% wt loss within 1 month (or 10% in 6 months) OR No wt stabilization or wt gain (i.e., continued wt loss)	> 5% wt loss in 1 month (or >10% in 6 months) OR No wt stabilization or wt gain (i.e., continued wt loss)
Nutrient Intake	No deficit OR Significant recent improvement	Definite decrease in intake	Severe deficit in intake
Nutrition Impact Symptoms	None OR Significant recent improvement allowing adequate intake	Presence of nutrition impact symptoms (Box 3 of PG-SGA)	Presence of nutrition impact symptoms (Box 3 of PG-SGA)
Functioning	No deficit OR Significant recent improvement	Moderate functional deficit OR Recent deterioration	Severe functional deficit OR recent significant deterioration
Physical Exam	No deficit OR Chronic deficit but with recent clinical improvement	Evidence of mild to moderate loss of SQ fat &/or muscle mass &/or muscle tone on palpation	Obvious signs of malnutrition (e.g., severe loss of SQ tissues, possible edema)

Global PG-SGA rating (A, B, or C) =

Appendix D: Study flyer



Invitation to participate in research

Pilot study: Determination and analysis of resting energy expenditure using indirect calorimetry of individuals with moderate sized burns.

Would you like to be part of a research project that is working to understand the energy needs of people with a burn injury?

This study will measure the energy use, throughout treatment and recovery, of patients with a burn injury. Participants will be asked to provide feedback on their experience with a short written questionnaire.

This research is being undertaken as we currently do not have a clear understanding of the energy needs of people with a burn between 5 and 15% or if the methods used to measure energy needs are acceptable by patients.

If you would like to be involved in this study one of the researchers will be available to speak with you and answer any questions that you may have.

Thank you,

Janica Bell

Principle Investigator

Janica Bell – Edith Cowan University

Associated Investigators

Dr Dale Edgar – Burn Service, RPH

W. Prof Fiona Wood – Burn Service of WA

Dr Angus Stewart – Edith Cowan University

A/Prof Philippa Lyons-Wall – Edith Cowan University

Location

Royal Perth Hospital



Appendix E: Patient information and consent form (PICF)

Fiona Stanley Hospital

Participant Information Sheet

Pilot study: determination and analysis of resting energy expenditure using indirect calorimetry of individuals with moderate sized burns

Principle Investigator

Janica Bell – Edith Cowan University

Associate Investigators

Dr Dale Edgar – Burn Service, RPH

W. Prof Fiona Wood – Burn Service of WA

Dr Angus Stewart – Edith Cowan University

A/Prof Philippa Lyons-Wall – Edith Cowan University

Location

Royal Perth Hospital

You are being invited to participate in this research study because you have recently been admitted to the Fiona Stanley Hospital (FSH) Burns Unit for treatment of a burn injury between 5 and 15% of your total body surface area. This study will investigate the use of an assessment tool known as **indirect calorimetry** to measure the resting energy needs of patients who have a moderate burn injury.

This information sheet explains the study and describes what will be involved should you decide to participate. Please read the information carefully and ask any questions you might have. You may also wish to discuss the study with a relative or friend.

You will be given a copy of this Participant Information and Consent Form to keep.

What is the purpose of this project?

After a burn injury there is an increase in the daily energy needs of the body for wound healing and recovery. Research investigating this increase in energy need has focussed on major burns of more than 20% total body surface area. The energy needs of moderate burns which are between 5 and 15% total body surface area is not well understood although most patients admitted to Royal Perth Hospital have a burn of this size.

To measure the amount of energy someone needs we can use an assessment tool known as indirect calorimetry. Indirect calorimetry has been used in research for more than 30 years to measure the energy needs of individuals with a burn injury. It is safe, non-invasive and accurate, and is recommended by international guidelines as the best method to work out the energy needs of burn patients. Although it is the best method to use we do not currently have a good understanding of the patient's experience of having indirect calorimetry measures completed.

In this study we want to find out what the energy needs are of people with a moderate burn using indirect calorimetry and understand the patient experience during measurements. The results of this study will assist clinicians in providing the right amount of nutrition to patients with a moderate burn.



Fiona Stanley Hospital

This project is a collaboration between RPH, FSH and Edith Cowan University. The results of this research will be used by the principle investigator, Janica Bell to obtain a Bachelor of Health Science Honours degree.

It is expected that 30 people will be involved in the study and all participants will have the same measurements completed. Some of the participants may also be involved in another study being conducted in FSH Burns Unit titled 'Does exercise training improve muscle strength and function after burn injury?'

What does participation in this project involve?

If you decide to participate in this study you will have your resting energy needs measured on three occasions using an indirect calorimeter. The three measurements will occur:

1. Within 72 hours of admission to the FSH Burns Unit;
2. 48 hours after surgery which occurs approximately 5 – 7 days after admission or 1 week after admission if you do not have surgery; and
3. 6 weeks after admission which is likely to be in the Burns Service outpatient clinic.

The third measurement, at 6 weeks after admission, will occur at the same time as your routine 6 week review appointment in the Burns Service outpatient clinic meaning that extra travel will not be required. Should you be discharged prior to the second measurement, at approximately 1 week after admission or 48 hours after surgery, the measurement will coincide with a routine visit to the Burns Service outpatient clinic.

The indirect calorimetry measurements will occur in the morning before breakfast as you need to have nothing to eat or drink (water is ok) for at least 4 hours prior to the measurement. Before the measurement and during the measurement you will be asked to lie in bed in a comfortable position in a relaxed, awake (not asleep) position and remain as still as possible. Just before the measurements start you will have a face piece such as a face mask or canopy-hood (see Figure 1 below) put in place. The face piece is designed to monitor the air you breathe in and air you breathe out, from this we can work out your energy needs. You will wear the face piece for about 30 minutes. You will be able to see your surroundings and the researcher will be able to see you during the measurement. You will also be able to hear what is happening around you and if you call out the researcher will be able to hear you.

After the first measurement you will complete a short written-survey which asks about your experience. It is expected that the survey will take less than 10 minutes to complete. If you require any assistance in completing the survey the researcher will be able to help.

We would also like to assess your nutritional status each time the indirect calorimetry measurement is completed. This will be done through two assessment tools which are commonly used by dietitians. The first is a hand-grip strength test using a tool called a dynamometer (see Figure 2 below). For this test you will sit on the edge of your bed or in a chair with your preferred arm for writing at a 90 degree angle. You will then be asked to squeeze the handle for three seconds as hard as you can and then release. This will be repeated twice with a short break in-between. This measurement will take about 5 minutes.

The other tool to determine your nutritional status is called a Patient Generated Subjective Global Assessment (PG-SGA). This tool is commonly used by dietitians and will take about 15 minutes to complete by a trained and experienced researcher. You will be asked a series of questions about your food intake, weight history, activity level, and nutrition impact symptoms which include nausea



Fiona Stanley Hospital

and dry mouth. The researcher will then complete a quick, non-invasive physical assessment to look at your muscle and fat stores.



Figure 1 – Example of an indirect calorimetry measurement using a canopy-hood



Figure 2 – Example of a hand grip strength measurement

What are the possible benefits of taking part?

This study aims to understand the use of indirect calorimetry to patients with moderate burn injuries. While there will be no direct benefit to you from taking part in the study the information collected may benefit others in the future.

What are the possible risks and disadvantages of taking part?

The indirect calorimetry, hand grip strength, and PG-SGA are all pain-free non-invasive tests. You may experience mild discomfort during the indirect calorimetry as you are required to remain still for the duration of the test and be fasted for at least 4 hours. Some people may experience discomfort while wearing the face piece. If you do experience discomfort during the measurement you will be able to communicate with the researcher and the measurement can be stopped immediately.

What will happen to information about me?

By signing the consent form you consent to the researcher collecting and using personal information about you for this project. Any information obtained in connection with this project that can identify you will remain confidential. All written information will be stored in a locked filing cabinet for a period of seven years, as required by law. All data stored in a computer will be accessible only by password known to the principle investigator. Both written and electronic data will be de-identified and will not contain any identifiable information such as your name, address, or telephone number.

Information about you will be obtained from your health records at FSH for the purpose of this research. By signing the consent form you agree to the research team accessing health records if they are relevant to your participation in this study.



Fiona Stanley Hospital

It is anticipated that the results of this study will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission.

In accordance with relevant Australian privacy and other relevant laws, you have the right to request access to the information collected and stored by the research team about you. You also have the right to request that any information with which you disagree be corrected. Please contact the research team member named at the end of this document if you would like to access your information.

Any de-identified information obtained for the purpose of this study may be used for future related research, subject to approval by a Human Research Ethics Committee.

Complaints and compensation

In the event that you suffer an expected or unexpected side effect or medical accident during this study that arises from your participation, you will be offered all full and necessary treatment by FSH.

Voluntary participation and withdrawal

Participation in any study is voluntary. If you do not want to take part, you do not have to. If you decide to take part and later change your mind you can withdraw at any stage without reason or justification. If you decide not to participate or you withdraw part-way through it will in no way affect your current or future care at FSH.

If you do withdraw consent during the project, the researcher will not collect additional personal information from about you, although personal information already collected will be retained to ensure that the results of the study can be measured properly. You should be aware that data collected by the researcher up to the time the participant withdraws will form part of the study results. If you do not want them to do this, you must tell them before joining the study.

What happens when the study ends?

The results of the study may be published in scientific journals or discussed at scientific meetings in the future. You can request a copy of the study report from the research team once it is written. If you would like a copy please inform the investigator.

Contacts for further information

If you would like further information about this project or if you have any medical problems which may be related to your participation, please contact the principle researcher, **Dr Dale Edgar, on (08) 9224 3566** or dale.edgar@health.wa.gov.au.



Fiona Stanley Hospital

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies. All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this project have been approved by the HRECs of RPH and Edith Cowan University.

If you have any concerns about the conduct of the study or your rights as a research participant, please contact Prof Frank van Bockxmeer, Chairman of the RPH Ethics Committee, via (08) 9224 2292 or rph.hrec@health.wa.gov.au and quote the reference number REG 14-122.



Fiona Stanley Hospital

Consent Form

Principle Investigator Janica Bell – Edith Cowan University
Principle Investigator Janica Bell – Edith Cowan University
Associate Investigators Dr Dale Edgar – Burn Service, Fiona Stanley Hospital
W. Prof Fiona Wood – Burn Service of WA
Dr Angus Stewart – Edith Cowan University
A/Prof Philippa Lyons-Wall – Edith Cowan University
Location Fiona Stanley Hospital

Declaration by Participant

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the study described in the Information Sheet.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this study as described and understand that I am free to withdraw at any time without affecting my future health care.

I understand that I will be given a signed copy of this document to keep.

I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to Edith Cowan University concerning my condition and treatment for the purposes of this project. I understand that such information will remain confidential.

Name of Participant (please print) _____

Signature _____ Date _____

Declaration by Study Doctor/Senior Researcher[†]

I have given a verbal explanation of the study, its procedures and risks and I believe that the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher[†] (please print) _____

Signature _____ Date _____

[†] A senior member of the research team must provide the explanation of, and information concerning, the study.

Note: All parties signing the consent section must date their own signature.



Fiona Stanley Hospital

Form for Withdrawal of Participation

Principle Investigator Janica Bell – Edith Cowan University
Associate Investigators Dr Dale Edgar – Burn Service, FSH
W. Prof Fiona Wood – Burn Service of WA
Dr Angus Stewart – Edith Cowan University
A/Prof Philippa Lyons-Wall – Edith Cowan University

Location Fiona Stanley Hospital

Declaration by Participant

I wish to withdraw from participation in the above research project study and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with Royal Perth Hospital.

Name of Participant (please print) _____

Signature _____ Date _____

Description of participant's decision to withdraw if communicated verbally to researcher.

Declaration by Study Doctor/Senior Researcher[†]

I have given a verbal explanation of the implications of withdrawal from the study and I believe that the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher[†] (please print) _____

Signature _____ Date _____

[†] A senior member of the research team must provide the explanation of and information concerning withdrawal from the study.

Note: All parties signing the consent section must date their own signature.

Appendix F: Study timeline

	March 2014	April 2014	May 2014	June 2014	July 2014	August 2014	September 2014	October 2014	November 2014	December 2014	January 2015	February 2015	March 2015	April 2015	May 2015	June 2015	July 2015	August 2015	September 2015	October 2015	November 2015	December 2015
Background																						
1. Literature review																						
2. Equipment preparation																						
Research proposal																						
3. Develop methods and proposal																						
4. Risk assessment management plan																						
5. Proposal presentation																						
6. Proposal review																						
Ethics																						
7. Submission to RPH HREC																						
8. Submission to ECU HREC																						
9. Submission to FSH HREC																						
Research																						
10. Subject recruitment																						
11. Measurements																						
Analysis																						
12. Foodworks data entry																						
13. Statistical analysis in SPSS																						
Thesis																						
14. Thesis write-up																						
15. Review and finalisation of thesis																						
16. Submission of thesis																						

Note. RPH = Royal Perth Hospital; HREC = Human Research Ethics Committee; ECU = Edith Cowan University; FSH = Fiona Stanley Hospital; SPSS = Statically Package for the Social Sciences