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OBESITY AND CHRONIC LOW BACK PAIN:

AN INVESTIGATION OF THE RELATIONSHIP AND POSSIBLE MEDIATING FACTORS

By

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Statement of Authentication

The work presented in this thesis is, to the best of my knowledge and belief, original except as acknowledged in the text. I hereby declare that I have not submitted this material, either in full or in part, for a degree at this or any other institution.

 …….

(Signature)

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Author Contributions to Published Works

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CB and PWMM participated in the design of the study and participant recruitment. CB completed all data collection procedures. CB performed data and statistical analysis, with assistance from PWMM where required. CB drafted the manuscript. JCS, BSC and PWMM participated in the drafting and editing of the manuscript. All authors read and approved the final manuscript.

Journal Article 2

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List of Abbreviations

A-L	Abdominal to lumbar adiposity ratio
A-L/BMI	Abdominal to lumbar adiposity ratio relative to body mass index
A-L/WC	Abdominal-to-lumbar adiposity relative to waist circumference
A-L/WHR	Abdominal to lumbar adiposity ratio relative to waist-to-hip ratio
BIA	Bioelectrical impedance analysis
BMI	Body mass index
CGRP	Calcitonin gene-related peptide
cLBP	Chronic low back pain
CRP	C-reactive protein
CT	Computed tomography
DXA	Dual-energy X-ray absorptiometry
EMG	Electromyography
FM	Fibromyalgia
FMI	Fat mass index
HAT	Head-arms-trunk
HRQoL	Health-related quality of life
IL-6	Interleukin-6
JCR	Journal Citation Reports
LBP	Low back pain
LES	Lumbar erector spinae longissimus

LR-	Negative likelihood ratios
LR+	Positive likelihood ratios
MF	Median frequency
MF-BIA	Multi-frequency bioelectrical impedance analysis
MRI	Magnetic resonance imaging
NMDA	N-methyl-D-aspartate
NSCLBP	Non-specific chronic low back pain
OA	Osteoarthritis
ODI	Oswestry Disability Index
RA	Rheumatoid arthritis
sEMG	Surface electromyography
SF-BIA	Single-frequency bioelectrical impedance analysis
SLR	Straight leg raise
Sn	Sensitivity
Sp	Specificity
%TBF	Total body adiposity percentage
TC-TBF	Total trunk adiposity circumference relative to percentage of total body adiposity
TNF-α	Tumour necrosis factor alpha
US	Ultrasound
VAS	Visual analogue scale
VIF	Variance inflation factor

WC	Waist circumference
WHO	World Health Organisation
WHR	Waist-to-hip ratio

Abstract

Background

Obesity and chronic low back pain (cLBP) are prevalent social and economic burdens with significant contribution to poor overall health. Previous research has viewed the two health conditions as separate research and clinical problems, but there is evidence of a relationship between them. However, combined obesity and cLBP research is limited and not well understood.

Aim

The aim of this thesis was to investigate the relationship between obesity and cLBP, and to explore the possible factors mediating that relationship.

Methods

A series of three explorative studies were employed to examine the relationship between obesity and cLBP. Study 1 investigated associations between BMI and exercise-related cLBP changes. Study 2 was an exploration of associations between adipose tissue distribution and cLBP. Study 3 investigated the effect of body mass distribution on a known postural task, and the possible mediation by movement of the lumbar spine or lumbar muscle endurance.

Results

BMI and BMI changes were not associated with cLBP, or successful predictors of cLBP changes. Regional adiposity, particularly the ratio of abdominal to lumbar adiposity, was associated with and

a significant predictor of cLBP. Body mass distribution was shown to result in poorer postural task performance, but mediation by spinal movement or muscle endurance was not confirmed.

Discussion

No significant relationships between BMI and cLBP were identified, indicating the reliance on BMI as an obesity measure may not be justified. The established associations between regional adiposity distribution and cLBP may suggest that adipose tissue is a key contributor within the obesity-cLBP relationship. Although mediation of spinal movement or muscle endurance was not supported in the experimental context used, the link between body composition and mass distribution with cLBP was further confirmed.

Conclusion

The work of this thesis supports evidence of a link between obesity and cLBP. Adiposity and body mass distribution have been implicated in this relationship. Future studies should continue to explore possible mediating factors between obesity and cLBP in a variety of research contexts.

Chapter 1: Introduction

1.1 The Problem

Obesity and chronic low back pain (cLBP) are both common and disabling health conditions.[1] Obesity refers to a state of increased fatness contributing to metabolic dysfunction.[2] The commonly accepted classification for obesity is a body mass index (BMI) ≥30.0kg/m^2, or waist circumference (WC) ≥88cm or ≥102cm for abdominal obesity in women and men respectively.[3] cLBP is the presence of low back pain (LBP; pain below the costal margin and above the gluteal fold) for a minimum of 12 consecutive weeks.[4] Both conditions contribute significant costs to society. The social and financial burden of obesity and cLBP can be attributed to expenses associated with healthcare of obesity-related chronic diseases, and costs incurred by various cLBP treatments.[1, 5-13]

The prevalence of obesity is on the rise, causing the condition to be labelled as an epidemic.[3, 14] Since the morbidity and mortality associated with obesity continues to increase, it has become a serious public health concern.[15] For example, cross-sectional studies have revealed that obesity in the United States accounted for 35.7% of the population in 2009-2010,[16] compared to 30.5% ten years earlier.[17] Obesity is also a prevalent condition in Australia, with 20-25% of the population reported as obese in 1999-2000.[18] Moreover, in a 2017 study modelling trends of the Australian adult population, obesity was projected to increase from 19.5% in 1995 to 35% by the year 2025.[19] Obesity rates in Australia have already tripled in the previous three decades (1980-2008),[20] with 1 in 4 of the population now classified as obese.[20] More importantly, obesity is a global health problem, with 12% of adults reported as obese globally.[21] If the post-2000 trends continue, the prevalence of global obesity has

been estimated to rise to 18% by the year 2025.[22] On average, the world's population is said to become >1.5kg heavier per decade.[22] In an age-standardised analysis of adult obesity from 1975 to 2014, the global obesity prevalence was found to have increased from 3.2% to 10.8%, and 6.4% to 14.9% in men and women respectively.[22] However, not only is it prevalent, but obesity is also a costly condition.[23] Total direct obesity costs in Australia have been previously estimated to equal $8.3 billion annually, which rose to $18.8 billion when overweight was also considered.[24] The health expenditure of individuals has recently been shown to coincide with obesity occurrence, whereby obese individuals exhibit approximately 30% higher expenditure than those of a normal weight.[20]

Obesity is considered to be the number one preventable public health concern in the United States.[2] For example, due to the risks and accelerating effect that obesity has on the metabolic syndrome and cancer, obesity may become detrimental to society if prevention and treatment are not carefully considered.[2] Many of the costs incurred by obesity are the result of complications of the condition and the comorbidities associated with it. Such problems can be attributed to the release of pro-inflammatory adipokines, in addition to the physical burden of additional body weight from excess adiposity.[2] For instance, adipose tissue affects the body via the space it occupies within and around bodily organs and structures.[2] Complications of obesity can include hypertension, endothelial dysfunction, cardiovascular disease, impaired glucose tolerance and type 2 diabetes mellitus.[15] Moreover, obesity can result in or put individuals at greater risk of comorbidities. These may include degenerative joint disease, obstructive sleep apnoea, increased pulmonary embolism, gallstone disease and gallbladder cancer, polycystic ovarian syndrome, preeclampsia and renal failure.[2] There are also gender-specific adverse effects of obesity, such as the possibility of amenorrhea, infertility, pregnancy complications and urinary stress incontinence in women.[2] Furthermore, obesity has been linked to emotional disorders, such as depression and bipolar disorder.[15] More importantly, obesity has been suggested to exist simultaneously to a number of chronic pain conditions.[25]

LBP is also prevalent, since it affects 10% of the world's population and has been recently ranked as the 7th leading disability in the world.[26] It is also the highest ranking disability in regards to the number of years lived with the condition.[26] Research indicates that approximately 80% of a given population will experience LBP at some point in their life.[1] Moreover, the majority of people that experience activity-limiting LBP will also suffer from recurrent episodes.[10] While most people recover from an episode, for a portion of the population LBP episodes become chronic.[1] The impact of LBP on health care systems in western society arises from the chronicity of the condition. cLBP is a common health problem in the western world, with 10.2% of people affected by the condition, regardless of gender, age or race.[1] cLBP is also on the rise, with a survey of the United States population observing a 162% increase in the condition from 1992 to 2006.[1] cLBP places a large economic burden on society, due to work absenteeism and treatment-related expenses.[10, 13] Such cLBP treatments include physiotherapy, chiropractic, massage, prescribed and over-the-counter drugs, osteopathy, acupuncture, psychology, naturopathy and occupational therapy.[13] The socioeconomic burden of the condition is so pronounced that there is said to be "general pessimism surrounding the prognosis of cLBP."[27] For example, in a systematic review of the costs associated with LBP, the indirect cost of lost work productivity was the greatest overall expense.[27] In Australia specifically, loss of income and treatment costs associated with cLBP are estimated to be $9.17 billion dollars annually.[13]

Past research on obesity and pain have been two entirely separate fields of study. For example, previous studies on obesity have investigated a variety of topics. These include the effect of diet and exercise,[28-31] obesity epidemiology and physiology,[2, 18] measurements of obesity,[3, 14, 32-36] and relationships to other health conditions such as diabetes and insulin resistance,[37, 38] bone density reduction,[39] sleep disturbance[40] and cancer.[41] In contrast, much of the previous back pain research was generalised to LBP and commonly focused on factors such as neuromuscular control,[42-56]

psychosocial factors[57-60] and the most effective treatment type.[51, 61-66] However, in more recent years the two separate fields of research of obesity and pain conditions have been merged together. This research crossover is significant because of the finding that people in chronic pain are often obese,[67] and those who are obese are often in pain.[14 68] For example, obese individuals have been found to be at a greater risk of pain induced by headaches.[69] As a result, there have been suggestions of common physiological pathways underpinning both obesity and pain conditions.[67, 70] More importantly, there is evidence of a specific relationship between obesity and cLBP[23, 71-80] that warrants further exploration.

1.2 The Content and Context of this Thesis

The obesity-cLBP relationship has commonly been evidenced via an association between BMI, a measurement commonly used to indicate overweight and obesity,[3, 14] and cLBP.[23, 81] However, it is unknown if obesity is a true causal factor,[75, 77] or rather indirectly contributes to cLBP.[67, 70] It may be possible for obesity to exacerbate or prolong existing cLBP, through the provocation and persistence of pain symptoms. This thesis aimed to investigate the relationship between obesity and cLBP by initially confirming an association between the two conditions, and thereafter to explore possible factors mediating that association.

Obesity was examined as more than a basic condition of body mass or simplistic measurements such as BMI, but rather a problem of adipose tissue and its impact on the body. Furthermore, this thesis discusses oversights of past research, particularly the previously unconsidered body mass distribution. Therefore, this research looked to investigate the mediating factors between obesity and cLBP, including adiposity and mass distribution. It also considered the effect of adiposity on postural task performance in cLBP individuals. Collectively, these themes will bring about an enhanced understanding of the relationship between these two disabling and costly health conditions, and what it may signify for future research and treatment possibilities.

1.3 Thesis Overview

Figure 1.1 illustrates the outline of experimental studies conducted within this thesis, for the purpose of fulfilling the primary aim to investigate the relationship between obesity and cLBP.

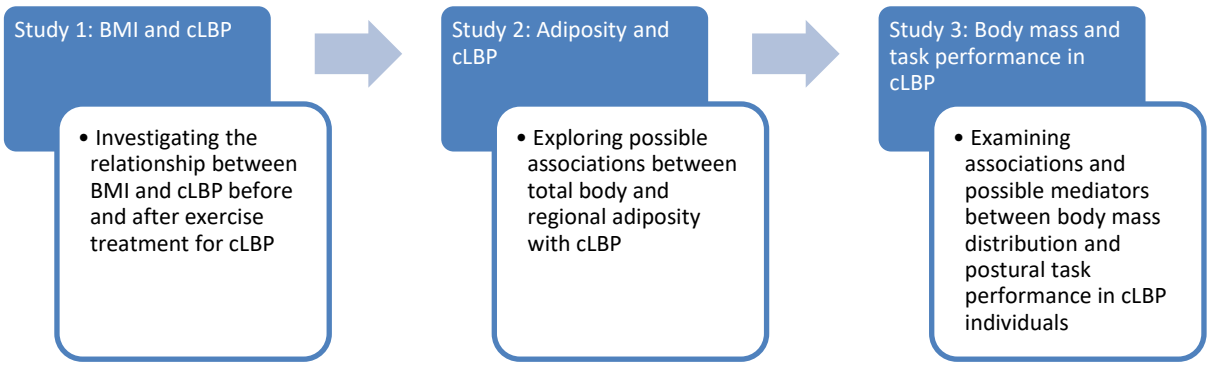

Figure 1.1 Outline of experimental studies contained within this thesis

1.3.1 Study 1: Examining relationships between body mass index and chronic low back pain before and after exercise

Since a relationship between obesity and cLBP has been previously suggested,[6, 23, 78] there is a rationale for this relationship to be further explored. In past studies, the emphasis has been on the use of BMI as a measurement of obesity in cLBP research.[23, 81] However, no studies have examined the relationship between BMI and cLBP prior to and immediately following an exercise intervention. Such research is important, as exercise is a commonly prescribed treatment for those suffering from cLBP.[82-86] Therefore, the first objective of this thesis was to investigate the relationship between BMI and changes in pain and disability levels among cLBP participants following an exercise program.

1.3.2 Study 2: Investigating associations between adiposity and chronic low back pain

Despite its frequent use, the BMI measurement has been previously criticised for its inability to discriminate between fat and fat-free mass within the body.[73, 80] Such limitations of BMI are important to consider regarding the obesity-cLBP relationship, since higher levels of adiposity (fat mass) have been linked to pain.[80] Furthermore, centrally-located visceral adiposity has been associated with pain conditions such as fibromyalgia (FM),[87] in addition to other medical pathologies[88] and obesity-related disorders.[89, 90] Consequently, simplistic weight indices such as BMI may be surpassed by adiposity-specific obesity measurements. Moreover, there is a lack of research on the potential links between adiposity and its bodily distribution with cLBP. There are various possible factors that may mediate a relationship between adiposity and cLBP. Such explanatory variables may include adiposity-stimulated inflammation,[80, 91-93] or the increased mechanical load on the spine.[80, 94] While it may plausible for adiposity distribution to be associated with cLBP, research into this relationship and its possible mediators is currently lacking. However, before investigation into obesity-cLBP mediation can be pursued, associations between adipose tissue and cLBP must first be confirmed. Therefore, the second objective of this thesis was to explore the relationship between total body and regional adiposity with cLBP, using alternative measurements to BMI.

1.3.3 Study 3: Exploring the effect of body mass distribution on task performance in the obesity-chronic low back pain relationship

It is also reasonable to believe that obesity (particularly abdominal adiposity) may have an effect on pain development and postural task performance. For example, perhaps increased abdominal mass may induce back pain through greater gravitational pull on the lumbar spine, as a result of spinal movement. This acute lumbar flexion may then promote excessive activation of spinal extensor

muscles to maintain balance, and consequently increase tissue strain on the lumbar spine region.[95] Furthermore, the task-specific lumbar flexion and increased muscle activation may result in a faster rate of lumbar muscle fatigue. Since increased lumbar flexion is known to coincide with LBP,[94] it is possible that greater abdominal mass may heighten pain experienced in a postural task. However, this notion is yet to be explored. Therefore, the third objective of this thesis was to explore the effect of body mass distribution on pain development, muscle fatigue and spinal movement in a postural task.

1.4 Summary

Past research on obesity and pain conditions has provided evidence of a relationship between obesity and cLBP. However, the nature and potential mechanisms of this relationship are yet to be determined. It is currently unknown if BMI is related to changes in cLBP following exercise, if adipose tissue distribution is related to cLBP, and if mass distribution has an effect on pain and task performance in cLBP individuals. Therefore, this thesis aims to confirm a relationship between obesity and cLBP, and investigate possible contributing factors to the relationship.

1.5 Experimental Objectives and Hypotheses

1.5.1 Thesis objectives

- To investigate associations between BMI and changes in pain and disability levels among cLBP participants following an exercise program.
- To assess associations between total body and regional adiposity and cLBP using alternative methods to BMI.
- To examine associations and mediating factors between body mass distribution and postural task performance in people with cLBP.

1.5.2 Thesis hypotheses

- Greater abdominal adiposity, particularly visceral, will be associated with increased self-reported pain and disability in cLBP individuals.
- cLBP individuals with greater abdominal adiposity will exhibit greater spinal movement, a faster rate of lumbar muscle fatigue, and acute flexion-induced pain development during a postural task.

1.6 Significance and Originality of the Research

Both obesity and cLBP are disabling conditions, with significant costs to the lives of individuals and society as a whole. Obesity is a known contributor to pathophysiological and metabolic disorders, and may exacerbate existing medical conditions. Similarly, cLBP is a social and financial burden to the western world. It is a common chronic health condition, affecting numerous countries worldwide and is a major cause of work absenteeism.

Not only is the link between obesity and pain still relatively recent, but there has been minimal combined research on obesity and cLBP. Moreover, previous research lacks consideration of body mass distribution in the obesity-cLBP relationship. It is possible that body mass distribution is a crucial factor previously overlooked in cLBP research, which may help explain why after 20 years of research the etiology of cLBP still remains unknown.

Chapter 2: Literature Review

2.1 Background

2.1.1 Physiology of obesity

Obesity is characterised by excess adipose tissue contributing to the dysregulation and dysfunction of the body and its associated components.[2] The excessive storage of fat as adipose tissue results in the release of free fatty acids,[96] causing lipotoxicity in both adipose and non-adipose tissues alike.[2] For this reason, obesity is often involved in the pathophysiology of organ dysfunction (including the liver and pancreas) and is known to contribute to the metabolic syndrome.[2, 25, 96, 97] Furthermore, the release of free fatty acids also results in the dysregulation of glucose metabolism causing insulin resistance from insulin receptor dysfunction.[2, 96] Consequently, this promotes the production of further glucose, causing hyperglycaemia and creating a cycle of dysfunctional insulin and glucose production and metabolism.[2] The adverse impact on normal glucose and lipid metabolism brought about by the positive energy balance of excess adipose tissue is a known contributor to the insulin resistant state embodying type 2 diabetes mellitus.[2, 15, 18, 98]

Due to the rise in obesity, the focus on and importance of adiposity has increased.[15] The normal function of adipocytes (fat cells) is the synchronised management of triglyceride synthesis (lipogenesis) and storage, with its rate of breakdown (lipolysis).[15] The way in which obesity impacts normal lipid and glucose regulation is via the secretion of large amounts of adipocyte-produced cytokines, or adipokines (proteins produced from fat cells).[2, 96, 97] These cytokines are known to

contribute to vascular dysfunction, atherosclerosis and inflammation.[2] In a holistic context, this disordered metabolic state causes organs and body systems to dysfunction, worsens the metabolic syndrome and accelerates cancer conditions.[2] As a result, the comorbidities to obesity are numerous, particularly through the effect obesity has on the normal functioning of organs and body systems.[2] Such systems include the liver, and cardiac, pulmonary, endocrine, immune and reproductive systems.[2]

2.1.2 Physiology of pain

Pain is an unpleasant sensory and emotional experience that is highly subjective and is associated with actual or potential tissue damage to the body.[92, 99, 100] In most cases the pain experience process begins in the body's periphery, where nociceptors detect noxious stimuli and transmit the pain signal to the brain via the spinal cord.[99-101] This stimulation of peripheral nociceptive receptors, termed primary sensitisation, results in the release of magnesium ions and subsequent activation of N-methyl-D-aspartate (NMDA) receptors, causing expansion of the pain receptive field and lowering of the depolarisation threshold.[92] It is possible for the repetition of this peripheral response to pain to occur, which may be through a continual pain-provoking stimulus or an increased intensity of painful stimuli.[92, 99] In such instances hyperalgesia follows, which is the increased pain response to an already painful stimulus.[92] The repetition of the primary pain response and continual nociceptive afferent barrage to the spinal cord then leads to central (secondary) sensitisation.[92] Consequently, the receptive field of NMDA receptors is further expanded, and a progressive accumulation of the overall pain response takes place in the dorsal horn neurons of the spinal cord.[92] Since each neuron can synapse with several thousand additional neurons, the level of pain is further amplified.[92] Therefore, the end result of repeated central sensitisation is the maladaptive chronicity of pain,[92, 99] which often displays the characteristics of a disease by its debilitating and unrelenting nature.[100]

2.2 The Beginning: A Link Between Obesity and Pain

There is a growing body of evidence to suggest a relationship between obesity and pain.[67] For example, the presence of pain is a highly prevalent complaint to healthcare providers,[14, 67] whereby 50% of obese patients seeking treatment also report a moderate to severe level of pain.[14 68] Previous research has identified a consistent linear relationship between increasing obesity and the reporting of pain.[70] In a study on individuals in the general population, it was found that the trend between obesity and pain became more apparent at each level of obesity (class I, II and III), whereby individuals at higher levels of obesity were more likely to report pain in increasing numbers of locations around the body.[70] In particular, pain complaints were more common with increasing BMI.[67] Research into obesity and pain conditions is not a new area of study, but is increasing in popularity since both obesity and chronic pain are on the rise.[68] Research has shown that obesity is a common comorbidity to conditions of chronic pain,[67] and that people who are overweight or obese are more susceptible to an increased occurrence of chronic pain conditions. Moreover, linear trends between BMI and chronic pain have also been shown, with up to a 254% greater rate of recurrent pain among those with morbid obesity (BMI≥40) compared to people of normal weight.[67] A recent review by Okifuji and Hare (2015) highlighted the commonality of obesity among chronic pain sufferers of varying nature, including widespread pain, FM and osteoarthritis (OA).[67] Within these chronic pain populations, several indicators of overweight or obesity have been linked to pain, including BMI, fat mass and waist circumference.[67] Obesity was also a proposed risk factor for future pain presence and persistence of arm, low back and widespread pain.[67] To further compound the problem, chronic pain was a frequently reported reason for increases in weight.[67] Several pain conditions have been explored in the context of a relationship to obesity.

Significant associations between obesity and pain conditions have been identified and supported by past research, including headache or migraine,[23, 69, 102-106] back pain,[23, 70-74, 76, 78-80, 106-113] chronic pain,[23, 110, 114-117] neck or shoulder pain,[70, 78, 110] abdominal pain,[23, 106] lower extremity pain,[70, 106] FM,[23, 118-123] OA[117, 124-131] and rheumatoid arthritis (RA).[132-137] Obesity is also a known or potential risk factor for future development of certain pain conditions, such as LBP,[14] OA,[14, 68] FM[68] and RA.[68] In a twin-based study, it was found that overweight and obese twins were 1.3 to 3.0 times more likely than those of a normal weight to report pain diagnoses and symptoms, including LBP, headache or migraine, FM, abdominal pain and chronic widespread pain.[23] Among adults, LBP, FM and arthritis are the most commonly suffered chronic pain conditions,[68] with OA and LBP being the most frequently researched conditions of co-occurrence to obesity.[14] OA is the most widespread form of arthritis and causes those with the condition to suffer from joint pain and localised inflammation.[68] Obesity is a known risk factor for OA, in particular that located in the knee.[68] For instance, there is a 4-fold higher prevalence of knee OA among obese adults when compared to non-obese adults.[14] While the exact mechanisms responsible are not well understood, cartilage degeneration from metabolic effects has been a suggested possibility.[68]

Moreover, evidence of a relationship between obesity and other pain conditions, such as headache or migraine, has been well-documented.[69, 103, 105, 138] For instance, morbidly obese individuals were found to have twice the risk of suffering from severe headache pain when compared to those of a normal weight.[69] Obesity has also been linked to other chronic health conditions such as FM[23, 118-123] and RA.[132-137] FM has no known cause and is a chronic pain condition characterised by widespread musculoskeletal pain and stiffness, physical fatigue and multiple other symptoms affecting activities of daily living.[68] Similarly, obesity is also a risk factor for the development of RA, an autoimmune disease characterised by disability, joint pain and chronic inflammation.[68] While research linking RA with obesity is inconclusive, a significant association between the two conditions has been identified

in the past with regards to alterations in body composition.[68] It is believed that the accumulation of adipose tissue plays an important role in this disabling and degrading disease.[68]

Back pain is another condition that has been linked to obesity. For instance, in a recent cross-sectional study of nine countries investigating the relationship between obesity and back pain, significantly higher odds ratios for back pain were identified among five (Finland, Russia, Poland, Spain, South Africa) of the nine included countries when classed as obese or morbidly obese by BMI.[109] LBP in particular has also been researched in the context of its co-occurrence with obesity.[14] The condition of LBP is classified as acute if the duration of symptoms is less than 6 weeks, with subacute between 6 weeks and 3 months, and chronic occurring for greater than 3 months.[14] Janke et al. (2007) suggested there was inconclusive evidence linking excess weight with LBP, due to ambiguity surrounding the possibility of a direct relationship, the strength of the relationship if one is present and the conditions under which such a relationship may exist.[14] They concluded it remains unknown if the relationship between obesity and LBP is causal, and raised the notion that varying definitions of LBP among research studies makes deductions challenging.[14] However, a relationship between obesity and LBP has been demonstrated in the past, mainly with the use of BMI as an obesity measure.[71, 74, 76, 78, 139] Moreover, recent research has found that individuals reporting high levels of pain intensity in the previous six months had significantly higher mean total body adiposity than those that reported no pain.[80] Furthermore, increased adiposity (total body, upper and lower limbs, trunk, android and gynoid) was associated with higher levels of LBP intensity and disability.[80]

In addition to general adult populations, research has also shown links between obesity and pain complaints and diagnoses among specific populations, such as veterans.[14, 67] Furthermore, the presence of pain in obese populations is implicated across multiple age groups, including children,[67, 106, 140] adolescents,[67, 106, 140] and the elderly.[67, 110, 116] For example, there are clear linkages between

obesity and knee OA among young, middle-aged and older adults.[14] In a cross-sectional study of 840 participants aged 70 years and over, obesity was significantly associated with the likelihood of chronic pain across most areas of the body including the head, neck, shoulders, back, arms and hands, legs and feet, pelvis, and abdomen.[116] In a sub-sample of the same aging study, the presence of abdominal obesity was found to double the likelihood of chronic back, hip, knee, leg or upper extremity pain.[110] Similarly, higher rates of overweight and obesity have been observed in children and adolescents with chronic pain, which may contribute to activity limitations among young people.[106] Moreover, the negative effects of obesity on health-related quality of life (HRQoL) among youth populations has been reported.[140] For instance, the reductions in quality of life brought about by the simultaneous occurrence of obesity and LBP is suggested to be intensified in children and adolescents when compared to adults.[68] Of greater consequence, the state of being overweight or obese early in life is now a known risk factor for pain development at later stages.[14]

Together with the greater presence of pain with increasing levels of obesity,[70] the array of pain conditions obesity is linked to, and the multiple population groups this relationship exists in, it may be the health implications associated with the co-existence of obesity and pain that is most important. For example, the combination of reduced physical function associated with overweight and obesity, in addition to the presence of chronic pain, has been suggested to be both the cause and consequence of obesity comorbidities, such as OA, sleep apnea, type 2 diabetes mellitus and psychosocial disorders.[68] Moreover, the impact of pain through the increased frequency of pain-related disability and reduced physical functioning has been specifically recognised among obese patients.[141] In addition, obesity has been linked to poorer quality of life and impaired functional capacity in people suffering from chronic pain conditions.[68] While this health impact may be specific to certain pain conditions, such as through the significant reductions in quality of life with simultaneous occurrences of LBP and obesity,[68] it is clear that when various chronic pain conditions

(including FM, OA, RA and LBP) are paired with obesity, those patients usually exhibit poorer physical function.[68] Not only is quality of life negatively impacted,[14] but the co-occurrence of obesity and pain has detrimental overall health consequences, ultimately resulting in increased mortality rates among this population.[67] It has been previously suggested that the obesity-pain relationship may be exacerbated by the concurrent effects that sedentary living and excess weight have on each other.[68] For example, a lack of physical activity contributes to obesity and directly or indirectly increases pain and disability, thereby further reducing physical activity.[68] While a possible dose-response relationship between BMI and pain with resulting negative consequences on HRQoL has been identified, it was concluded that further clarification was required.[14]

2.3 The Focus: Obesity and Chronic Low Back Pain

While overweight and obesity have been linked to various pain pathologies as outlined above, there is also evidence of a relationship between obesity and LBP that is chronic in nature.[23, 71-80] For example, individuals classified as overweight or obese may be at greater risk of cLBP development than those of a normal weight.[78, 81] In a twin-based study on overweight, obesity and reporting of chronic pain symptoms and diagnoses, cLBP was the most commonly diagnosed condition (26% of study participants).[23] Both overweight and obese individuals were significantly associated with cLBP, and remained significant after adjustment for age, gender and depression.[23] Irrespective of such findings, discrepancy exists among the literature regarding gender. For example, Heuch et al.[74] identified a significant positive association between BMI and chronically-occurring LBP[74] that was present across both genders. Conversely, associations between obesity measures and cLBP have not been consistently significant for men in other studies,[78] particularly after adjustment for confounding variables.[73] While associations between obesity and cLBP have been observed across both genders,[74] some studies have suggested the association is stronger among women.[68, 74] A proposed explanation for this discrepancy included possible hormonal or adiposity differences between men and women.[68]

Relationships between obesity and cLBP have been identified across a range of anthropometric measures. For example, in a 10-year prospective study of Norwegian men and women, overweight or obese individuals (measured by BMI) were at a greater risk of chronic pain in the lower back when compared to those of normal weight.[78] However, the study design was admittedly limited by BMI being measured at baseline only, so changes within the 10-year follow-up period were not considered.[78] Higher prevalence of cLBP among men and women with increasing measures of WC, waist-to-hip ratio (WHR) and BMI was also found in a study on the Dutch population.[73] In this study, women with increased WC had greater odds of reporting cLBP than those with lower WC

measurements.[73] Similar results were seen for BMI and WHR, whereby increased relative risk of cLBP was observed with greater WHR and BMI values.[73] Both men and women with indications of overweight, obesity or heightened non-specific indices of adiposity were found to be at an increased risk of cLBP.[73] After adjustment for confounding variables, these relationships between BMI, WC and WHR with cLBP remained significant for women only.[73] Such gender-based differences may be better understood if adipose tissue is found to play a role in cLBP development.

In a matched-control study on Japanese people with cLBP, it was found that WHR was significantly higher among women with a negative straight leg raise (SLR) test compared to age- and gender-matched healthy controls.[112] It was concluded that central obesity, as depicted by an elevated WHR, may be a risk factor for cLBP among women aged 45 to 69 years.[112] While this study was limited to an older population, it was specific to cLBP and assessed several anthropometric and body composition variables. Such variables included BMI, percentage of total body adiposity (%TBF), lean body mass and WHR, across both subjects and control participants.[112] Within the female sample assessed, %TBF was reported to be significantly higher in cLBP participants with negative SLR compared to controls.[112] BMI was not associated with negative SLR cLBP participants.[112] Interestingly, in addition to WHR and increased %TBF, reductions in lean body mass of the trunk and lower extremities relative to body weight were correlated to negative SLR cLBP.[112] Therefore, it was suggested that the presence of central obesity and loss of trunk muscle mass may be implicated in the risk of non-sciatic cLBP in women aged 45-69.[112]

Despite such evidence, it is difficult to draw firm conclusions from previous research into the relationship between obesity and cLBP. This is due to the limited number of studies on cLBP specifically, as opposed to generalised LBP. For example, in alignment with much of the previous research, BMI has been shown to predict LBP recurrence.[68] Furthermore, both BMI and increased fat

mass have been associated with greater LBP intensity and disability.[68] Moreover, there is a need for greater clarity of LBP or cLBP distinction in some studies. In the paper just mentioned,[68] LBP is referred to in the context of a chronic condition. However, the distinction is not consistently clear, being coupled with citations from both LBP and cLBP research. It may be argued that this lack of clarity within the LBP research, both chronic and otherwise, hinders greater advances in understanding the relationship between obesity and pain conditions such as cLBP. In addition, conflicting findings have also been evident among past studies, including multiple literature reviews within this area (Table 2.1).

Table 2.1 Reviews on the relationship between overweight/obesity and pain (including LBP)								
Ref.	**Article Author/s**	**Pub. Year**	**Type of Article**	**No. of included studies**	**Years included**	**Outcomes of Interest**	**Main Findings**	**Author/s Conclusions**
[68]	Arranz et al.	2014	Literature Review	Not specified	2000 – 2013	Effects of obesity on chronic pain, particularly QoL and functional capacity.	Obesity is associated with increased prevalence of LBP. Causal relationship between high BMI and LBP is controversial.	Overweight/obese people have higher prevalence of chronic pain co-morbidities (FM, OA, RA, LBP) and worse functional capacity and QoL. More research needed on pathophysiologic mechanism of excess body weight and pain
[142]	Garzillo & Garzillo	1994	Literature Review	7	1970 – 1994 (?)	Association between obesity and LBP.	Poor correlation between weight/BMI and LBP (especially in lower 80% of BMI. Good correlation in upper 20% of BMI.	Possible association between obesity and LBP in upper quintile of obesity only. No evidence of temporal relationship.
[75]	Leboeuf-Yde	2000	Systematic Literature Review	65	1965 – 1997	To determine if body weight is associated with LBP and if the link is causal.	Significant positive association between weight or relative weight and LBP in 21 of 65 (32%) studies. No obvious consistency of findings among large general population-based studies.	Not enough evidence to determine if causal relationship between body weight and LBP.
[14]	Janke et al.	2007	Literature Review	Not specified	2000 – March 2006	To examine the relationship between weight and pain with 4 focuses: 1) commonly researched pain	Relationship between obesity and pain (eg. OA, possibly LBP) supported by cross-sectional studies. Overweight/obesity early in life possible risk factor for	Likely relationship between overweight or obesity and pain (based on available evidence). More

						conditions in co-occurrence to overweight/obesity (incl. LBP); 2) relationship between HRQoL, pain and obesity; 3) weight reduction effects on pain, and pain treatment on weight reduction; 4) possible explanatory mechanisms.	LBP/OA development (longitudinal studies). Possible dose-response relationship between BMI and pain. HRQoL negatively impacted by obesity-pain co-occurrence.	information needed on the nature of the relationship.
[97]	Shiri et al.	2010	Meta-analysis	33	1966 – May 2009	Association between overweight/obesity and LBP, and estimate magnitude of association.	Obesity associated with increased LBP prevalence in last 12 months, cLBP or LBP seeking care (cross-sectional studies). Overweight people have higher LBP prevalence than normal weight. Obese people have higher prevalence than those overweight. Obesity associated with increased LBP incidence ≥1 day in past 12 months (cohort studies).	Overweight/obesity increases the risk of LBP.
[77]	Mirtz & Greene	2005	Literature Review	8	1990 – 2004	To determine if there is a causal link between obesity and LBP.	Direct association for obesity as risk factor in 2 studies. No association in 2 studies. Several studies not in agreement to cause/association. Several studies unable to clarify BMI adequately.	BMI<30 minimal risk of LBP. BMI>30 moderate risk of LBP development. BMI>40 at high risk. No definitive causal link between obesity and LBP. Data appears controversial.
QoL, quality of life; HRQoL, health-related quality of life; FM, fibromyalgia; OA, osteoarthritis; RA, rheumatoid arthritis; LBP, low back pain								

Multiple reviews have concluded there is insufficient evidence to confirm a relationship, causal or otherwise, between body weight or obesity and LBP.[14, 68, 75, 77] There seems to be a trend of inconsistency among reviews on body weight or obesity and LBP, regarding reporting of populations, outcome measurements and study findings. Factors possibly impacting on the ability to draw conclusions from the research include varying body weight measurements,[75] and difficulty deciphering LBP definitions.[14, 75] For example, the lack of standard definition and diagnostic certainty for the LBP condition has been raised.[14] As a result, the frequency and chronicity of pain measurement differs among studies and makes the relationship between overweight or obesity and LBP challenging to discern.[14] Moreover, cLBP definitions vary even among reviews. A meta-analysis defined cLBP as pain lasting for greater than 7-12 weeks, or an excess of 30 days within the previous 12 months.[97] In contrast, a separate review referred to cLBP as LBP occurring for more than 3 months.[14] This variance has arisen in a simple definition of cLBP between two papers reviewing similar research, irrespective of the multiple other possible sources of disparity in outcome measurement, definition or reporting. Therefore, it is not difficult to identify why evidence of an obesity-cLBP relationship may appear controversial at best.

Another identified limitation of past research is poor BMI classification.[77] This has included unclear distinction between overweight and obesity, and various BMI cutoff points.[97] For example, some studies examined in a meta-analysis deviated from the World Health Organisation's (WHO) BMI value of ≥30.0 for obesity[3] by using a BMI≥27.0 or ≥28.5 cutoff.[97] For this reason, the meta-analysis included a combined overweight/obese category of BMI ≥25.0, with studies using BMI≥24.0 for overweight/obese or ≥28.5 for obese also included.[97] This variance of obesity classification generates confusion and may produce inaccuracies among study findings. The meta-analysis also revealed that 13 out of 24 cross-sectional studies relied on self-reported height and weight,[97] which further raises the possibility of error. The authors proposed that the lack of consistency of overweight and obesity

cutoff points as per the WHO guidelines, in addition to several studies failing to report frequency, severity or case definition of LBP, may lead to possible underestimation of the strength of the obesity-LBP association.[97] Another limitation raised by multiple reviews is that LBP is typically a reference to a symptom rather than a confirmed diagnosis.[14, 77] This may further hinder the understanding of a possible association between obesity and LBP, and make determining a possible cause and effect more challenging.[77]

It has been revealed that few studies have explored causal relationships between weight or obesity and LBP, chronic or otherwise.[14] Although several reviews have supported the possible existence of a relationship between overweight or obesity and LBP,[14, 68, 75, 77, 97, 142] there is little evidence within the current scientific community to indicate a direct relationship.[14] Moreover, it appears generally accepted that existing findings are inconsistent and inconclusive, so additional research is needed to determine the extent of the relationship.[14, 75, 77, 142] Some suggested reasons for the lack of knowledge about the relationship between overweight or obesity and LBP include a weaker association between the two conditions than previously hypothesised.[14] Another possibility was poor classification of the term 'LBP' and its reference to a non-specific disease with unknown etiology.[14] Additional suggestions included research into weight and LBP being secondary exploratory work with a lack of hypothesis-driven research questions, or the existence of other mediating factors between weight and LBP requiring further investigation.[14] It has also been suggested that this association may be bi-directional, in which obesity could either be a cause or consequence of LBP.[97]

Such reviews reveal important considerations omitted from previous literature, which hinder the ability to deduce the exact relationship between obesity and cLBP. As mentioned earlier, there have been several different LBP definitions and body weight measurements used in the past.[75] For example, the variance of reported frequency and chronicity of pain between studies has made

conclusions regarding obesity and LBP difficult to decipher.[14] Exploring such relationships may continue to be problematic until a standard definition for LBP has been firmly established, and the certainty of diagnosis is widely and consistently used. Moreover, one of the issues with body weight measurements in previous studies is the poor classification of BMI,[77] which is a common measure of obesity among LBP literature.[71, 74, 76, 78, 139] This was previously alluded to in a meta-analysis, which raised the issue of multiple BMI cutoff points amid studies, and unclear delineation between overweight and obesity.[97] This is an important issue, as some studies have only identified associations between obesity and LBP in the higher percentiles of BMI.[142] Furthermore, since the prevalence of chronically-occurring LBP rises with increasing WC, WHR and BMI,[73] such cutoff points of measurements like BMI may be of great significance. In addition, there is a general consensus that further research is required to better understand this relationship and the potential factors that may be interceding it.

2.4 Physical Activity and the Obesity-cLBP Relationship

Physical activity may be another important consideration in the obesity-cLBP relationship. In a literature review of 16 studies on exercise for cLBP in overweight or obese populations, exercise was found to be a beneficial method of management for obesity and obesity-related comorbidities.[143] Moreover, a study comparing different types of exercise (general aerobic and strengthening exercise, aquatic exercise, home-based aerobics) to non-active controls confirmed that physical activity was more effective than inactivity for pain and disability improvement.[144] A recently proposed pathway explaining links between exercise, obesity and LBP suggests inactivity may contribute to worsening LBP symptoms and increased weight gain, whereas exercise may improve pain and physical function and assist in weight management.[143]

Physical inactivity may be further implicated in the obesity-cLBP relationship, since it is associated with an increased risk of LBP.[78, 111, 145] More specifically, the highest risk of LBP has been found in obese individuals who maintain sedentary behaviours, with the greatest effect shown in WC-measured abdominal obesity rather than BMI-derived general obesity.[111] In contrast, no risk of LBP was identified in obese participants who were physically active.[111] It was concluded that the impact of physical activity levels on LBP may be altered by obesity, or that both obesity and sedentary behaviours may amplify the influence of each factor on LBP occurrence.[111] However, these results were only found in radiating LBP and were not observed among those with non-specific LBP.[111]

Associations between physical activity and odds of LBP among overweight and obese individuals have also been identified in other studies.[78, 145] For example, weekly leisure-time exercise was shown to be inversely associated with cLBP risk.[78] Combined effects of BMI and exercise showed that ≥1 hour of exercise on a weekly basis reduced cLBP risk in both men and women regardless of baseline BMI.[78]

However, obese men and women who were inactive had a higher risk ratio for LBP compared to their active counterparts (in both obese and healthy participants).[78] It was proposed that a small amount of exercise per week (1-1.9 hours) could reduce cLBP risk,[78] which has also been supported by other research.[145] For example, increasing time spent performing moderate physical activity by an average of 17.6 minutes per day resulted in a 32% lower LBP risk for overweight individuals.[145] Moreover, risk of LBP was reduced by 38% in morbidly obese individuals from minimal increases in moderate physical activity (1.3-2.1 minutes/day).[145] Therefore, physical activity was concluded to be an independent predictor of LBP, after statistical removal of BMI.[145] The most predictive effects of physical activity on LBP were within moderate- and high-intensity ranges, but the effects were small.[145] However, when BMI was included, sedentary and moderate physical activity time had the greatest influence on LBP.[145] Such findings may suggest that inactivity and consequently obesity may be a potential result of LBP, or that obesity may lead to LBP and inactivity, or alternatively that increased sedentary living may result in either LBP or obesity.[143, 145] It has been further suggested that exercise may bring about a protective effect on LBP, particularly among overweight and obese populations.[145] This was supported by a review comparing different types of exercise for LBP, in which significant improvement in pain, physical function and muscular strength were observed after 2-4 months of resistance training, aquatic exercise or Pilates.[143] One possible rationale for a protective effect of exercise may the result of reductions in low-grade systemic inflammation brought about by physical exercise.[78, 111]

A further consideration in the obesity-cLBP relationship may be physical activity for the purpose of, or independent of, weight loss, which is a typical goal among overweight and obese populations.[143] There is currently inconclusive evidence to indicate whether weight loss is the determining factor for LBP improvements following exercise. More specifically, individuals who are overweight or obese are advised to remain physically active regardless of weight reduction,[111] since greater risk of radiating

LBP has been associated with obesity but not excess body weight.[111] However, there is also existing evidence supporting weight loss outcomes among obese individuals with LBP.[146] Following a 52-week weight loss program on obese adults, both weight and BMI were reduced, with trends towards LBP reductions and disability improvements.[146] Moreover, positively-associated trends for clinically meaningful reductions in LBP were identified with higher percentage reductions in BMI at week 53.[146] Authors suggested those who had observed and continued weight loss were more likely to reduce LBP symptoms, with a possible explanation being the attenuation of low-grade systemic inflammation from combined effects of weight loss and increased daily physical activity.[146] While weight loss was suggested to be the primary factor eliciting LBP and disability improvement, a key limitation of the study was the lack of a control group.[146] Given the substantial duration of the study, the acknowledged inability to observe general severity of LBP among obese adults and natural fluctuations in weight or weight loss[146] limited the generalisability of the study.

With consideration of the existing research on possible influences of physical activity on the obesity-cLBP relationship, the limited number of studies in this area makes it difficult to draw firm conclusions. Moreover, variance among studies regarding physical activity or exercise modalities, LBP definitions and types, and methods of obesity measurement also restrict the ability to compare such findings.

2.5 The Experimental Context

Before extrapolating potential mediating pathways in the obesity-cLBP relationship, the existing body of evidence suggesting mediators in the relationship between obesity and pain must first be examined. As highlighted earlier, previous research has included general studies on obesity and pain as well as more specific studies on LBP, chronic pain or cLBP. In this section, all research within the context of obesity and pain will be considered. In the past it has been suggested that the association between obesity and pain may be bi-directional.[116] Alternatively, it may be possible for obesity to merely be a marker for a true causal factor, or combination of factors.[72] For example, the association between obesity and greater risk of pain may not be directly linked, but rather a mediation of one or more interrelated variables.[67, 70]

2.5.1 Previous research into mediating factors between obesity and pain

Two commonly considered mechanisms underlying a relationship between obesity and pain are those of a mechanical or inflammatory nature. For example, it has been suggested that excessive weight among children may bring about greater risk of pain and injury through increased stress on the musculoskeletal system.[106] Much of the research surrounding obesity and pain has focused on LBP. While some evidence exists to support a causal link between obesity and LBP,[71] the possible contribution of obesity on LBP development or vice versa is a contentious topic.[108] Yet, it is known that LBP symptoms are worsened by the co-occurrence of obesity.[108] Moreover, it has been suggested that obesity places an abnormal load on the lumbar spine and may therefore predispose it to mechanical disadvantage.[72] For example, the heightened load on the body brought about by excess body weight may have a detrimental mechanical impact on the spine.[71] It was suggested that the

prolonged state of excess body weight may place greater compressive loading on intervertebral discs or create additional spinal stress during functional tasks, both of which may lead to LBP.[73] More importantly, there have been further suggestions that obesity-induced mechanical loading of the lower back region may be dependent on body morphology, or somatotype,[147] whereby the greatest effect would be observed among those with central adiposity.[147] In a recent study on body segment inertial parameters, increases in trunk moments of inertia and radii of gyration were observed among people with central adiposity.[147] They discovered a 20% increase in body mass distribution to the trunk relative to that of normal BMI, and concluded that central adiposity-dependent mechanical loading was observed.[147] The effects of greater centrally-accumulated adiposity on body mechanics may also include gait and shock absorption changes, predisposing the spine to further strain.[73] For instance, it was suggested the lumbar spine may be subject to increased compressive or shear forces as a consequence of obesity.[97] A final suggestion was an association via disc degeneration, whereby obesity leads to reduced spinal mobility and consequential disc nutrition interference and triglyceride alteration.[97] Obesity may then lead to increased risk of degeneration of intervertebral discs and therefore a heightened chance of suffering from LBP.[97] For example, Yang et al. observed associations between increased abdominal and sagittal diameters with greater odds of severe lumbar disc degeneration.[148]

Another consideration is that adiposity may play a role in the obesity-pain relationship as a result of systemic inflammation. For instance, it is known that adipose tissue is an active organ with a role in inflammation regulation.[68] More specifically, adipose tissue is involved in the production of cytokines contributing to a pro-inflammatory state, such as interleukin-6 (IL-6) and tumour necrosis factor alpha (TNF-α).[79] In turn, C-reactive protein (CRP) is released which given its multiple sources of production, acts as a non-specific inflammatory marker of adipose tissue.[79] With respect to associations between obesity and pain pathologies, adipose tissue has been previously implicated.[149-151] For example,

adiposopathy ('sick fat' syndrome) is a state of elevated BMI and chronic systemic inflammation, whereby metabolic changes occur within the body in response to increasing adiposity.[152] Research suggests that the presence of adiposopathy is the determining factor for musculoskeletal pain to coincide with BMI increases.[152] Moreover, there are established links between adiposity and specific pain pathologies. For example, associations between obesity and RA have been more attributed to body composition changes than BMI.[68] It was proposed that the accumulation of adipose tissue, perhaps triggered by metabolic dysfunction as a result of the chronic inflammatory state of RA, is believed to play a key role in the disease.[68] Inflammation and the metabolic syndrome have also been proposed mechanistic possibilities in the association between overweight/obesity and LBP via adipose tissue distribution.[97] There are multiple potential mediating pathways between adipose tissue and back pain, including adiposity-induced metabolic changes.[80] For instance, the obesity-LBP link may exist by means of chronic systemic inflammation, in which the proliferation of pro-inflammatory cytokines and acute-phase reactants accompanying obesity may give rise to pain.[97] Another proposed mechanism of action was a "pathomechanical pathway"[97] between the metabolic syndrome and LBP, given the existing associations between several components of the syndrome and LBP including abdominal obesity, hypertension and dyslipidemia.[97]

Not only has there been established links and proposed mediating pathways between obesity and pain conditions such as LBP, but research has also extended this relationship to pain chronicity. Although only generalised to the elderly population, it was observed that those with abdominal obesity were close to twice as likely to experience chronic pain.[116] Moreover, this finding was independent of several other relevant factors to the obesity-pain association, including high-sensitivity CRP, psychological disorders, pain co-morbidities and remaining metabolic syndrome components, thereby suggesting some other mechanistic link between obesity and pain.[116] Obesity has been associated with a twofold greater likelihood of chronic pain in people aged 70 years and

over when compared to people of normal weight, which increases to four times more likely in those severely obese.[110] One possibility that may explain the association between obesity and chronic pain is the increased mechanical demand on joints with a weight-bearing role.[110] However, there may also be other factors, given obesity has been found to have significant associations to both weight-bearing and non-weight-bearing body sites.[110, 151] The mechanisms responsible for the overweight or obesity and chronic pain relationship are not well understood, but evidently may be the result of multiple factors.[23] For example, people who are overweight or obese are more susceptible to a pro-inflammatory state, which is compounded by an increased prevalence of chronic pain conditions.[68] Research suggests that the onset and persistence of chronic pain may in part be due to chronic systemic inflammation.[68] As previously suggested, the effect that obesity has on the body may be explained by adipose tissue leading to pain susceptibility from altered metabolic processes.[116] In contrast, the chronicity of pain may stimulate the secretion of cortisol, which plays a role in central obesity.[116] There is also a rising body of research that musculoskeletal condition development may be instigated by metabolic considerations, such as through cytokine release and adipokine mediation.[80] Specifically, the release of pro-inflammatory factors amplifies the inflammatory state of the spine, thereby intensifying the pain experience, and possibly instigating a chronic pain state as a result of consequential tissue damage.[80]

It is known that increased levels of inflammatory markers such as TNF-α, IL-6 and CRP have been linked to obesity, rendering the body to a state of pro-inflammation.[110] Therefore, it has been proposed that inflammation may be a mediating factor between obesity and chronic pain.[110] Yet the directionality of the relationship remains unknown.[110] For example, pain prevalence may be augmented by obesity if pro-inflammatory cytokines are found to cause greater predisposition to pain.[110] A possible suggestion for the chronicity of LBP among many individuals is that the excess weight of obesity exacerbates existing pain to the point that it becomes persistent.[76] However, it

seems to be more specifically related to central adiposity, since distribution of adipose tissue around the body is more closely related to cLBP risk than overall BMI.[112] Additionally, elevated WC and WHR have also been associated with occurrence of the chronic disease FM in women, but BMI and weight were not.[87] The authors suggested the possibility that there may be a "bias toward central adiposity" in obese women with FM.[87]

Therefore, it has been concluded that the mechanisms responsible for the interacting relationship between obesity and chronic pain in the adult population may include mechanical, metabolic or behavioural factors.[140] The obesity-pain relationship may be attributed to physical loading considerations but also systemic mechanistic factors, since fat mass rather than fat-free mass was important to multisite pain.[149] The inflammatory substances released from metabolically-active adipose tissue have demonstrated effects on joint structures, nociceptive pain pathways and chronic pain development and progression.[149] Moreover, the mechanical musculoskeletal impairment brought about by excess weight and possible chronic inflammation may lead to reduced physical function and chronic pain presence.[68] Such factors have been proposed as both the cause and consequence of obesity comorbidities, such as OA, sleep apnea, type 2 diabetes mellitus and psychosocial disorders.[68] To conclude, it has been established that excess body weight and obesity contributes to chronic pain, with two commonly proposed mechanisms responsible for this interaction. The suggested mechanisms are mechanical stress on the musculoskeletal system and increased pain from systemic inflammation, yet a combined mechanical and systemic effect mediating the obesity-pain relationship may also be possible.[14, 68]

2.5.2 Consideration of the possible mediators in the relationship between obesity and cLBP

Inflammation is a proposed mediator of the association between obesity and chronic pain.[110] Distribution of adipose tissue, an active organ and known contributor to inflammation regulation,[68] is more strongly related to the risk of cLBP than BMI.[112] As a result, it is reasonable to believe that the association between obesity and cLBP may be based on the inflammatory response of the body, and the metabolic interaction between adipose tissue and pain receptors. Moreover, this interacting physiology of adipose tissue and pain may further stimulate chronic low-grade inflammation and promote the persistence of pain, since obesity has been previously implicated in the exacerbation and prolonging of existing LBP.[76] Alternatively, it is also possible that the obesity-cLBP relationship may be the result of a mechanical mediation pathway, such as changes in spinal positioning, or the consequence that extra body mass and its distribution around the body has on the pain experience. There is also support for such a mechanical mediation, since previous research has indicated that obesity-chronic pain links may be explained by greater demand on weight-bearing joints.[110] Additionally, the excess body weight of obesity places an abnormal load on the lumbar spine,[72] such as increased compression forces on intervertebral discs.[73] Such forces may then predispose the spine to mechanical disadvantage.[72]

2.5.2.1 A metabolic pathway: Inflammation

Inflammation may mediate the obesity-cLBP relationship, since an altered immune response involving chronic low-grade metabolic inflammation ('metaflammation') has been proposed to be the linking factor between type 2 diabetes mellitus, metabolic syndrome, insulin resistance, endothelial dysfunction and cardiovascular disease,[153] and underlies most if not all forms of chronic disease.[91] For example, there are multiple inflammatory markers of significance to both obesity and migraine pathophysiology, including CRP, Il-6, substance P, TNF-α, mast cells, macrophages, orexins and calcitonin gene-related peptide (CGRP).[25] Such inflammatory markers have been shown to increase migraine frequency, severity and duration.[25] Since past evidence indicates a relationship between obesity and migraine[69, 103, 105, 138] with relevant inflammatory markers to that relationship,[25] it is logical to conclude that there may also be a relationship between obesity and other chronic pain conditions such as cLBP. For example, there is evidence of dysregulation and dysfunction of pain processing pathways in cLBP in a similar manner to other chronic pain states, such as FM.[154, 155] Several conditions with similar underlying pathophysiological dysfunction have been previously termed as 'central sensitivity syndromes', which includes tension-type headache, migraine, interstitial cystitis, FM and temporomandibular disorders.[156] The commonality of pain processing dysfunction among known disorders, as mentioned above, therefore makes the possibility of similar dysfunction in cLBP plausible. More specifically, metaflammation may mediate the obesity-cLBP relationship (Figure 2.1). This may occur through metabolic and physiological processes occurring within adipose tissue, in which increased adiposity stimulates inflammation and further promotes the persistence of chronic pain.[80, 91-93]

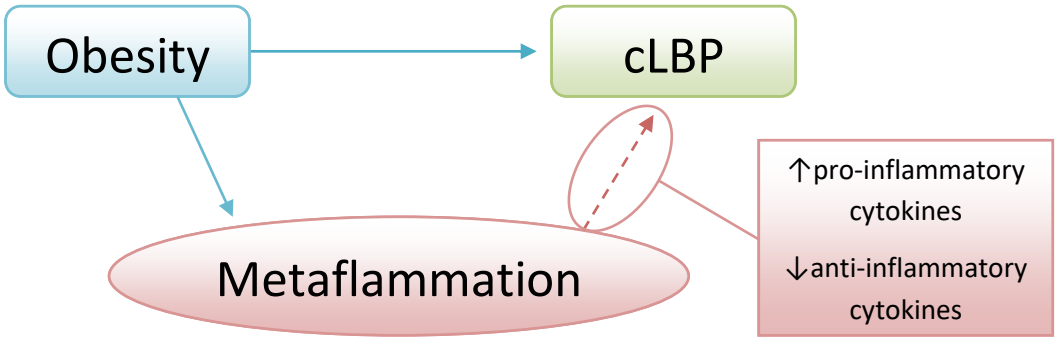

Figure 2.1 A proposed model of the inflammation-related mediation in the relationship between obesity and cLBP. Solid arrows indicate evidence of a relationship. Dotted arrows indicate proposed relationships.

Although cLBP does not appear to exhibit the widespread pain evident in other conditions,[154] it does seem pathophysiologically similar to FM[157] and may lead to FM development.[158] Metabolic processes associated with excess adipose tissue may explain the relationship between adiposity and back pain and disability.[80] As mentioned earlier, adipose tissue is not only an organ passively storing excess energy, but is actively involved in inflammation regulation.[68] It is also thought to be directly involved in the pathophysiology of obesity-related diseases.[96] For example, the overflow of adipocyte cells into excess visceral and ectopic (blood, liver and muscle) stores is known to initiate a process of metabolic dysfunction, contributing to insulin resistance and end-stage disease.[91] Furthermore, a state of positive energy balance typically due to physical inactivity or excessive caloric intake, would lead to this accumulation of adipose tissue and subsequently adipocyte hypertrophy.[93] The consequence of adipocyte hypertrophy is then macrophage and T cell infiltration.[93] Such infiltration stimulates increased production and release of pro-inflammatory cytokines (eg. TNF-α and Il-6) and reduced production and release of anti-inflammatory cytokines (eg. adiponectin).[93] As a result, the release of pro-inflammatory cytokines through activated immune cells may produce heightened nociceptor activity[101] and hyperalgesia.[92] As previously discussed, NMDA receptor activation and lowering of the

depolarization threshold then leads to an amplification of the overall pain response.[91] The possibility that chronic low-grade inflammation could result from such pathophysiological processes, may then support the proposed metaflammation-mediated relationship between obesity and cLBP.[93]

It is reasonable to believe that the inflammatory state initiated by excess adiposity can lead to the persistence of cLBP. For instance, it has been suggested that metabolic processes related to increased adiposity may be involved in the relationship between fat mass and back pain.[80] The mechanism responsible for this relationship may be the inflammation incurred from the hypertrophy of adipocytes, which promotes the release of pro-inflammatory adipokines (adipocyte-specific cytokines) from adipose tissue.[93] Additionally, the increased perception of pain that has been found in obese individuals,[159] is said to be caused by a local release of chemical substances from neuronal and non-neuronal cells including immune cells.[92] Since immune cells are known to release cytokines[101] and possibly induce hyperalgesia,[92] adipose tissue may be responsible for repeated primary sensitisation and expansion of the pain receptive field. As previously mentioned, repetition of the peripheral pain response leads to central sensitisation and further amplification of pain levels.[92] The end result of such processes is the suggested chronic pain state.[92] Therefore, the relationship between obesity and cLBP may be attributed to hyperalgesia and central sensitisation driven by adiposity-derived inflammation.

2.5.2.2 A mechanical pathway: Abdominal to lumbar adiposity

A second proposed mediation pathway for the obesity-cLBP relationship is that of a mechanical nature (Figure 2.2).

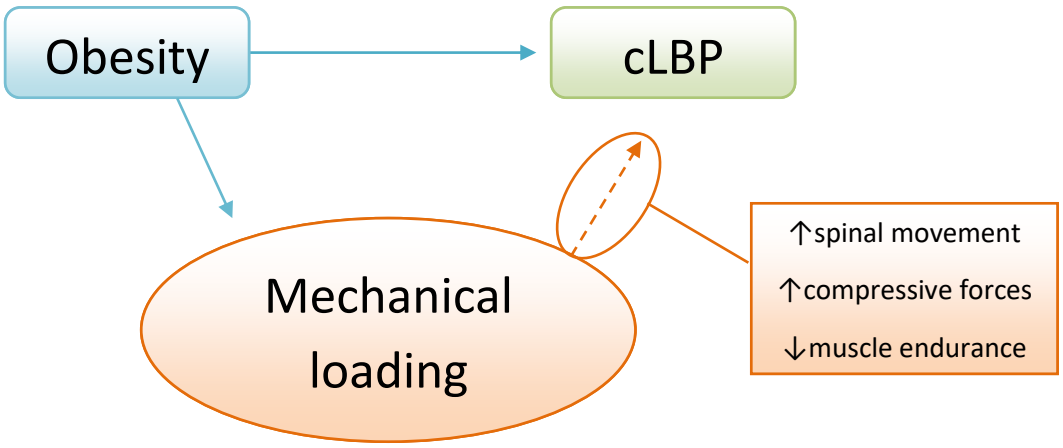

Figure 2.2 An alternative model of a possible mechanical mediation between obesity and cLBP. Solid arrows indicate evidence of a relationship. Dotted arrows indicate proposed relationships.

Mechanical loading may be an important consideration in the obesity-cLBP relationship. For example, it is possible that an association between spinal positioning and pain development exists. This may be evidenced by a pilot study comparing cyclists with and without flexion-provoked non-specific cLBP (NSCLBP). In this study, a trend towards greater flexion and axial rotation of the lower lumbar spine was observed among those with NSCLBP.[95] The testing protocol required participants to cycle until the onset of LBP (pain group) or until general discomfort prevented further riding (non-pain group).[95] Although the findings failed to reach statistical significance, a large effect size indicated a trend towards greater flexion in the lower thoracic region of the spine. Moreover, when considered in conjunction with lower lumbar flexion angles, it was suggested there may be a clinically relevant difference in thoracolumbar flexion between pain and non-pain groups.[95] Similarly, a study on industrial workers identified that those with flexion-related LBP adopted sitting postures with

increased posterior pelvic tilt when compared to healthy controls.[94] The LBP participants also sat with the lumbar spine closer to end of range flexion,[94] thereby habitually adopting a more pain-provoking posture.[94] An additional study on adolescents with NSCLBP also observed the tendency to adopt sitting postures of greater pain provocation.[160] In that study, adolescents with extension-related NSCLBP sat in postures of greater lumbar lordosis, when compared to the flexion-related pain and control groups.[160] O'Sullivan et al.[94] suggested that such habitual loading of tissues already sensitised to pain responses may lead to further nociceptive sensitisation, resulting in greater tissue loading and a possible chronic pain state.[94] The notion of pain sensitisation was also discussed by Burnett et al.,[95] whereby the observed movement pattern adopted preceded the task-induced onset of pain.[95] Given the presence of an existing sensitisation to movement and loading associated with lumbar flexion, the authors suggested cyclists in the pain group appeared to adopt patterns of movement that further increased the flexion and rotational strain on the lumbar spine.[95] It was proposed that rather than a reflexive mechanism to pain occurrence, the pattern employed was an "inherent movement fault."[95] Spinal movement has also been observed during a trunk extension task among healthy male participants.[161] During the final 30% of the return movement to upright, the lumbar spine and hip consistently exhibited an over-corrective shift into 2-6 degrees of flexion.[161] Although the study only included healthy participants, it was proposed that the identified "phenomenon" of an overcorrection phase may be beneficial in understanding lumbar spine and hip kinematics in LBP sufferers.[161]

In addition to the lack of statistical significance resulting from riding posture and small sample size,[95] further limitations exist within the cycling study. The observed spinal movement trends coincided with pain development, indicated by the increase in pain reported at the end of the ride compared to baseline scores.[95] However, the study claimed to cease testing at the onset of pain and also refers to LBP participants reaching a point where cycling had to cease.[95] Therefore, there is insufficient

information provided to deduce whether this is at onset of pain or not. The study also requires greater clarification with respect to grouping. For example, groups were claimed to be matched as closely as possible by age, height, weight and BMI,[95] but later by 1) total ride time, 2) ride position and 3) height.[95] As a result, it is unclear precisely how groups were matched. A further limitation was that neither of the cycling or sitting studies included the consideration of adiposity and body mass distribution. Although cycling and seated postures are body weight-supported tasks, it is possible that such factors may relate to the obesity-cLBP relationship by other means of mechanical loading.

The mechanical loading associated with increased shear or compressive forces on the lumbar spine from excess adiposity may be one such factor. The lumbar spine is known to transmit the mechanical forces of compression to the lower body, to maintain upper body support during daily activity.[162] It is possible that excess abdominal adiposity may heighten the gravitational pull on the lumbar spine and contribute to compensatory lordotic positions. Moreover, such alterations to normal daily posture may result in greater repetition or magnitude of compressive spinal loading, which is known to increase the risk of intervertebral disc injury.[163] For example, an in vitro examination of axial compressive loading and flexion/extension motion effects on porcine spines, showed a greater likelihood of disc herniation with increased repetition of flexion/extension moments.[163] This damage was observed with minimal joint compressive forces and was intensified with higher axial compression magnitudes.[163] Moreover, increases in cyclic flexion/extension moments were suggested to generate cumulative and progressive damage.[163] It may then be possible for the obesity-cLBP relationship to manifest through adiposity-induced compressive loading or flexion/extension moments. Further support may be evidenced by another porcine study, in which models were exposed to combinations of compressive forces, postural deviation and shear displacement to produce vertebral joint failure.[164] The study found that ultimate shear failure force was influenced by the deviation of posture from neutral, or by compression-related vertebral joint height reduction.[164]

Shear failure force was highest during extension (less space between articulating facets) and lowest during a flexed posture (facets further apart).[164] Although ultimate shear failure force was impacted by increased compression,[164] postural deviation was deemed of greatest consideration since flexion reduced the vertebral joint's capacity to tolerate shear loads.[164] A third porcine specimen study examined compressive loads and rotational torques to assess the impact of loading history and failure posture.[165] This study also identified decreased compressive loading tolerance with full spinal flexion.[165] More specifically, they identified a 43-63% lower yield point (the load at which stiffness decreased and injury originated) in a position of spinal flexion when compared to neutral posture.[165] A 23-47% lower ultimate compressive strength (maximum tolerable load before deformation increased) was also observed.[165] Such studies may validate the possibility of a mechanical loading mediation in the obesity-cLBP relationship, since greater spinal movement may coincide with increased pain[94, 95] and reduced loading tolerance.[163-165]

The effects of compressive loading have been further demonstrated in a study on creep and recovery responses of human intervertebral discs of the spine.[166] The study compared two experimental loads, a slow compression load of 2000N over 30 minutes and a rapidly applied creep load of 1000N held for 4 hours.[166] The recovery time was found to be longer than the duration of loading, and the rate and duration of loading had an observed effect on recovery.[166] For example, the discs exposed to the 30-minute load exhibited an immediate recovery of 70% of displacement, but only a 20% recovery was observed immediately following the 4-hour loading.[166] The mechanism of action was suggested to be time-dependent, whereby the externally applied forces of the creep loading impacted the osmotic pressure enough to initiate a rapid expulsion of fluid.[166] In the unloaded recovery phase, only the osmotic pressure was present to facilitate the movement of fluid back into the disc so recovery was slower.[166] Since the creep loading utilised in the study was representative of standing while holding an object, it may be possible to liken such loading to increases in body weight and particularly

that of greater abdominal adipose tissue. However, it remains unknown if this has an effect on pain experienced, since authors of the aforementioned cycling study rejected the possibility that back pain development results in the progressive deformation of spinal creep.[95] The rationale provided was that spinal posture was not modified as a reflex pain response during the cycling task.[95] Authors proposed that since back injury is increased with end of range strain, it may be possible for the trend towards increased flexion and rotation among pain group participants to be related to prolonged end of range strain.[95] Since further clarification with respect to the onset of pain and exact test cessation was needed in the study, it is difficult to confirm or refute this possibility.

It is also known that spinal stability is required for successful transmission of forces to the lower body, and that the degree of stability required is dependent on task demand and muscular involvement to prevent buckling under high loads.[162] This was demonstrated by a study using a lumbar spine model to estimate stability during three-dimensional dynamic tasks.[162] In this study, stability was found to be paramount during demanding tasks and increased with greater compressive forces.[162] In contrast, stability of the spine decreased when it was not needed as critically and during tasks with little demand on muscular activity, perhaps to reduce energy expenditure.[162] In these situations, the passive joint tissues such as discs and ligaments are believed to play an important role.[162] It was suggested that a loss of stability at any given moment would result in unexpected spinal displacement, triggering nociceptive input from nerve roots or surrounding connective and soft tissues.[162] The need for the recovery of spinal stability following displacement may then result in tissue overload.[162] The authors concluded that less stable and demanding tasks such as standing present a greater risk of buckling, particularly if lower passive joint stiffness is also present.[162] They also suggested that moments acting on the lumbar spine have to be balanced by musculature.[162]

Given the involvement of muscle force on the stability of the spine, there may be an underlying muscular mechanism contributing to the potential mechanical mediation of the obesity-cLBP relationship. For example, the distribution of body mass may play a role in spinal extensor muscle fatigue. More specifically, the greater abdominal adiposity may alter muscle recruitment strategies in functional body positions whereby posture is at play. It has been previously shown that people with NSCLBP display a trend towards increased muscle activation of some back extensors (erector spinae, multifidus) and abdominal muscles (rectus abdominis), with a reduction in the activation of other abdominal muscles (internal oblique) when compared to those without pain.[95] Since such trends were observed in the presence of greater flexion and rotation moments, it was suggested that alterations in muscle activation may indicate a consequential pain response. Alternatively, the authors also proposed a counteraction to lower back flexion and rotation moments via increased extensor moments.[95] For instance, during flexion the extensor muscles are required to produce an internal extensor moment to return the spine to an upright position, which is said to increase compressive forces on the vertebral joints.[164] Moreover, an in vivo study of the feline lumbar spine showed that cyclic loading resulted in greater lumbar spine muscle activity, with repetitive exposure leading to viscoelastic creep and pain.[167] The study involved 20 minutes of passive cyclic lumbar flexion to examine possible biomechanical and neurophysiological pathways in idiopathic low back and cumulative trauma disorders, commonly seen among workers performing repetitive lifting tasks.[167] Study findings indicated that the greater the loading magnitude, the slower the recovery time.[167] Moreover, even the minimum load of 20N was found to be sufficient to trigger the observed response.[167] It is also known that a prolonged state of static flexion causes changes to the flexion-relaxation muscle response, whereby the activity of the erector spinae muscles is heightened as a result of viscoelastic creep.[168] During flexion and extension movements of the lumbar spine, the synergistic balance of loading between passive viscoelastic structures and lumbar musculature is required to counteract gravitational forces.[168] If the forces produced by passive structures are not sufficient to support the weight of body structures against the force of gravity, the lumbar extensor

muscle activity must increase to compensate.[168] The consequence of this imbalance may then be the disruption of optimal function and over-activation of extensor musculature.[168] As suggested in the study on feline models of the lumbar spine, such increases in muscle activity may increase creep and pain development.[167] Furthermore, the study on industrial workers with LBP discussed earlier identified a reduction in the endurance of lumbar musculature in those with flexion-provoked pain when compared to pain-free controls.[94] They also found a significant association between decreased lumbar muscle endurance during the Biering-Sorensen test, and the increased posterior pelvic tilt observed during adopted sitting postures.[94] Therefore, muscle activation changes and reduced lumbar muscle endurance may be associated with movement of the lumbar spine, and play a role in the provocation of LBP symptoms. Since research has also shown that obesity is linked to increased fatigability in tasks involving gravity counteraction,[169] this possibility of a mechanical effect linking obesity with cLBP through muscle fatigue may be further strengthened.

2.6 Methods of Obesity Measurement

Within the context of the potential relationship between adiposity and cLBP, it is important to examine the various methods previously used to assess levels of obesity and adiposity.

Much of the previous obesity and cLBP research has relied on BMI as a measurement of obesity.[71, 74, 76, 78, 139] While BMI is a commonly used method for assessing the obesity of an individual,[3, 14] inadequacies of the measurement have been previously identified. Such inadequacy includes possible misclassification, resulting from a lack of distinction between fat and fat-free mass within the body.[73, 80] Given such limitations pertaining to the sole reliance on the BMI measurement, research has begun to investigate alternative methodologies for assessing body composition and adiposity, including bioelectrical impedance analysis (BIA)[33-36, 170-181] and ultrasound (US).[32, 90, 182-186] BIA is a method used to assess body composition and estimate an individual's percentage of total body adiposity, based on the principle of impedance or resistance to the flow of an electrical current through the body.[35, 173] Despite previous concern regarding the use of universally applied body composition measures to both lean and obese populations,[33] BIA has been shown to be a valid and reliable measure of total body adiposity (Table 2.2).[33-36, 173, 176, 178, 179, 187-193] For example, a 2008 study on body composition in obese and non-obese men and women observed strong correlations ($r>0.8$) between BIA and the reference method dual-energy X-ray absorptiometry (DXA).[33] Moreover, no statistically significant differences were identified between BIA and DXA for estimates of body composition, including %TBF, fat mass and fat-free mass.[33] However, the authors concluded that accurate estimates of changes in body composition remained in question.[33] Subsequently, a separate study also comparing BIA to DXA, examined the estimation of body composition changes following weight loss in young overweight women.[36] The results of measurements before and after a 10-week weight loss intervention revealed good agreement and no significant differences between BIA and DXA for body composition variables

(including body composition changes).[36] Although both single-frequency BIA (SF-BIA) and multi-frequency BIA (MF-BIA) assessments were shown to be accurate in terms of bias and limits of agreement, MF-BIA was considered to be superior to SF-BIA.[36] The reason provided was that SF-BIA tended to underestimate %TBF, whereas MF-BIA correlated more closely to DXA values.[36] They further emphasised that hand-to-foot electrode placement was more accurate than foot-to-foot arrangement.[36] Contrary to this, other studies have proposed SF-BIA to be of greater use.[35, 187] Moreover, some studies have concluded all methods of BIA tested to be reliable for body composition assessment.[188, 193] Although wide limits of agreement have been previously identified for the BIA method,[34-36, 187, 193] error values have been considered acceptable[192] and consistently reported at approximately 2% difference to the reference method.[34, 187, 189, 192, 193] Estimation errors for BIA have also been lower than the skinfold method.[188] Several studies have supported the use of BIA for group or population studies.[35, 190, 193] In a similar manner to BIA, other reference methods are not without flaws. DXA also has potential limitations,[187] despite its common use as a reference method.[33, 35, 36, 187, 189, 190, 193] For example, DXA testing is expensive and requires specialised equipment and trained technicians.[35] Comparatively, BIA requires little operator training,[194] is on par with skinfold thickness testing[194] and may be a more useful measurement than BMI at population level for the risk of obesity-related chronic diseases.[193] As such, BIA is a viable alternative for body composition assessment.[36, 190, 192]

Table 2.2 Validity and reliability studies of bioelectrical impedance analysis methods to comparative methods of total body adiposity measurement								
Ref.	**Author/s**	**Pub. Year**	**Population tested**	**N=**	**BIA method used**	**Comparison method**	**Main Findings**	**Author/s Conclusions**
[33]	Boneva-Asiova and Boyanov	2008	Obese and non-obese adult men and women	283	Foot-to-foot (Tanita TBF-215)	DXA	%TBF was not significantly different from DXA. %TBF from BIA was highly correlated with DXA-derived measurements for males and females BMI<30, BMI 30-35 and BMI≥35 (r=0.83-0.98, p<0.001). Correlations decreased for increasing BMI.	Good correlation between body composition parameters derived from BIA and DXA. Body composition indices by DXA were not statistically different from BIA and were highly correlated.
[34]	Chouinard et al.	2007	Overweight adults, aged 18-44 years	38	SF-BIA Foot-to-foot (Tanita TBF-305)	4C Model	No significant differences in %TBF between Tanita and 4C Model at baseline. Tanita overestimated %TBF changes by 0.9% in the placebo group when compared to the 4C model. Significant correlations were identified between %TBF at 0 and 6 months for Tanita and 4C model (r≥0.90, p>0.001). No biases between methods were found at 0 or 6 months. Both methods detected %TBF changes, but BIA results did not reach statistical significance.	The BIA method performed relatively well compared to the 4C model in the accuracy of detecting %TBF changes in overweight adults, but had wide limits of agreement at the individual level.
[35]	Pateyjohns et al.	2006	Overweight or obese men, aged 25-60 years	43	MF-BIA (ImpediMed SFB7, Imp-MF), SF-BIA (ImpediMed	DXA	There was good relative agreement between DXA and all three BIA methods, with significant correlations for %TBF (Imp-MF, r^2=0.69; Imp-SF, r^2=0.40; Tanita, r^2=0.44; all p<0.001). The	SF-BIA methods (Imp-SF and Tanita) may be useful in group comparisons, but use in individual body

					DF50, Imp-SF), SF-BIA (Tanita UltimateScale, Tanita)		absolute agreement between DXA and Imp-MF was poor (large bias, wide limits of agreement). Imp-SF and Tanita also had wide limits of agreement, but smaller bias than Imp-MF. There was no significant difference between DXA and Tanita values for %TBF.	composition assessment may be limited.
[178]	Ritchie et al.	2005	Older adults, aged 55 years and over	50	Foot-to-foot (Tanita, BF-556)	Hand-to-foot BIA (BIA 310)	Significant correlation (r=0.84, p<.001) between hand-to-foot BIA and Tanita for %TBF and the 2 means not significantly different. %TBF correlated to BMI, WC and age (all p<.01) for both methods.	Tanita BIA valid %TBF measure in older adults.
[36]	Thomson et al.	2007	Overweight or obese females, aged 18-38 years	24	SF-BIA (Tanita UltimateScale, Model 2000), MF-BIA (ImpediMed SFB7)	DXA	MF-BIA estimates showed good absolute agreement with DXA (small bias in %TBF), but wide limits of agreement, SF-BIA larger bias with wide limits for %TBF. During weight loss, MF-BIA and SF-BIA not significantly different to DXA. No significant difference between DXA and MF-BIA for body composition (p≥0.88), significant correlation between MF-BIA and DXA for %TBF (r^2=0.20, p=0.03). Significant difference between SF-BIA and DXA for body composition. Both SF-BIA and MF-BIA accurate for body composition changes when compared to DXA. Prior to weight change, both SF-BIA and MF-BIA showed moderate relative agreement for %TBF compared to DXA.	BIA methods useful and valid alternative to DXA, good absolute and relative agreement for change in body composition. MF-BIA superior to SF-BIA when compared to DXA.
[188]	Demura et al.	2002	Young Japanese males	50	Hand-to-hand (Omron HBF-300), hand-to-	Underwater weighing (A&D, AD-	Significant differences were observed between BIA and underwater weighing, with %TBF higher using BIA. Correlations	All BIA methods showed high reliability. Validity was

			aged 18-27 years		foot (Selco SIF-891) and foot-to-foot (Tanita TBF-102)	6204), sum of skinfolds	between BIA methods and underwater weighing were strong (hand-to-hand, r=0.708; hand-to-foot, r=0.878; foot-to-foot, r=0.747) (all p<0.05). All three BIA methods showed high reliability (r=0.999). BIA tended to over- or underestimate %TBF in individuals with low or high relative body adiposity. Estimation errors were lower for BIA methods when compared to the skinfold method.	highest using the hand-to-foot method of BIA. Correlation to underwater weighing was also high for hand-to-foot BIA, so this method of BIA is considered superior than the other two tested.
[191]	Loenneke et al.	2013	Male and female college students	21	Foot-to-foot (Tanita model TBF-350), hand-to-hand (Omron HBF-306C)	3-site skinfold thickness	There were no significant pairwise differences observed between repeat testing sessions (two visits on alternate days of the same week) for any of the methods tested. Pearson correlations ranged from r=0.933 to r=0.994 (p<0.001). Intraclass correlations ranged from 0.93 to 0.992. Minimal differences ranged from 1.8% for skinfold testing to 5.1% for TBF-350 (athlete mode).	Skinfold testing and the Omron (athlete mode) method were the most reliable methods of assessing (<2%) %TBF. The remaining methods produced minimal differences greater than 2%.
[187]	Aandstad et al.	2014	Male and female first-year military cadets	65	SF-BIA (RJL Quantum II), MF-BIA (Biospace Co. InBody 720)	DXA 6-7 site skinfold thickness	SF-BIA produced generally more reliable results than the skinfold method. MF-BIA had wider limits of agreement, but higher validity results in men compared to SF-BIA. MF-BIA underestimated %TBF by approximately 2% when compared to DXA.	The SF-BIA method was shown to be the most reliable and the most valid in women. In men, skinfolds or skinfolds and SF-BIA were the most valid. At an individual level, wide limits of agreement were

								observed in comparison to DXA.
[189]	Fornetti et al.	1999	College-age female athletes (aged 18-27 years)	132	Hand-to-foot (RJL 101A analyser)	DXA	High intraclass correlations were observed for BIA for single and repeat trial reliability. There were strong correlations between BIA and DXA. The prediction error was 1.8% for BIA when compared to DXA. Validity coefficients, standard error of measurements and total error values produced similar cross-validation results.	BIA is a valid and reliable method for estimating body composition in the population tested, provided the given equations are used.
[193]	Von Hurst et al.	2016	Adult males and females, aged 18 years and over	166	InBody 230 (Biospace Co.)	DXA and ADP	Excellent relative agreement was observed for BIA to the estimated true value. Strong correlations were found between BIA with ADP and DXA (r^2=0.88 and respectively r^2=0.92, but wide limits of agreement were observed. %TBF was consistently underestimated by 2% using the BIA method. Excellent reliability was shown for all methods using repeat measurements (<0.2% difference and small 95%CI).	All methods were shown to be reliable. There was excellent relative agreement between BIA and comparative methods, but bias and wide limits of agreement were observed for absolute agreement. BIA may be a valid method for use in research and population studies.
[190]	Kafri et al.	2014	Stroke and TIA patients	10, 40	MF-BIA (Maltron BioScan 920-2)	DXA	No significant differences in group means were found between BIA and DXA. Strong correlations were identified between BIA and DXA (%TBF for all BMI categories; r^2=0.631, p=0.006). No statistically significant differences were	Good agreement was shown between BIA and DXA. BIA may be of further use in research and clinical care.

							observed between means of repeated measures (average 2–10 measurements). Good reliability was shown using 80 measurement pairs.	
[192]	Moon et al.	2008	Healthy college-age men	31	RJL Quantum II	Siri 3C Model	BIA produced an acceptable total error value of 2.1%TBF and had the highest validity coefficient (r=0.91) and smallest limits of agreement of all field methods tested.	BIA is a valid and acceptable field method for the assessment of %TBF when laboratory methods are not available. Error values for BIA were acceptable (≤4%TBF).
BIA, bioelectrical impedance analysis; DXA, dual-energy X-ray absorptiometry; %TBF, percentage of total body adiposity; BMI, body mass index; WC, waist circumference; SF-BIA, single-frequency bioelectrical impedance analysis; MF-BIA, multi-frequency bioelectrical impedance analysis; 4C Model, Four-compartment model; 3C, three-compartment model; ADP, air displacement plethysmography; TIA, transient ischaemic attack								

Since the regional distribution of adipose tissue, particularly visceral adiposity,[88, 89, 195, 196] has been suggested to be more important than total body adiposity, it is necessary to acknowledge the various anthropometric and imaging methods used to assess regional adiposity. Anthropometric data includes WHR, WC and abdominal sagittal diameter, which are inexpensive and easily obtainable but have low accuracy and reproducibility.[186] Imaging techniques include computed tomography (CT), magnetic resonance imaging (MRI) and sonography or US. While CT and MRI are highly reproducible and CT is a reference standard for adipose tissue evaluation, both methods are expensive.[186] CT also involves ionising radiation, and MRI is less readily available and tends to overestimate adipose tissue deposits.[186] US on the other hand has showed strong correlation to visceral adiposity evaluation with CT methods, and is safe, cost-effective and accurate.[32, 186] US has been shown to be a valid and reliable method of assessing abdominal adiposity when compared to gold standard methods.[32, 90, 182-184, 186] It involves taking linear measurements of adipose tissue thickness based on anatomical references such as the linea alba.[32, 182] Unlike DXA, US can distinguish between visceral and subcutaneous adiposity.[32] Intra-abdominal adipose tissue thickness is a sonographic index used to measure visceral adiposity, which is highly reproducible and correlates well with CT.[186] It is defined as "the distance between the anterior wall of the aorta and the posterior surface of the rectus abdominis muscle."[186] Intra-abdominal adipose tissue thickness is correlated with cardiovascular risk factors, such as total and HDL-cholesterol, fasting glucose levels, triglyceride levels and fasting insulin.[186] It is considered to be the most reliable adiposity index, based on its confirmed reproducibility among multiple patient groups, including healthy, obese and diabetic populations.[186] Previous research has observed good accuracy for visceral adiposity and even stronger accuracy for subcutaneous measurements, when compared with CT.[32] It was also found that there was significant reproducibility for obese and non-obese patients, and excellent intra-operator reliability.[32] However, the comparison between total body and regional adiposity as opposed to BMI and other anthropometric measures, is yet to be investigated in the cLBP population.

2.7 Summary

It is possible that the missing link among all previous cLBP research may be the distribution of body mass, particularly that which is located in the abdominal region. For instance, the possibility of an inflammation-based mediating pathway between obesity and cLBP, may be a reason why abdominally-accumulated adiposity is paramount in the relationship. Alternatively, mechanical mechanisms may be responsible for the relationship between obesity and cLBP, such as through the effect that distribution of mass has on the body. For this reason, the studies included in this thesis are the necessary foundational steps to better define and understand the relationship between obesity and cLBP, and the potential factors mediating that relationship. It is plausible that the distribution of abdominal adiposity in cLBP individuals may be the uniting factor among obesity and cLBP research. Furthermore, adiposity distribution may link various elements of past LBP studies, including control of posture, spinal movement changes and task performance and fatigue.

While multiple potential mediating factors in the relationship between obesity and cLBP are discussed in this thesis, not all of them were investigated within the context of the PhD. This thesis will not cover a detailed metabolic investigation or manipulation, or the observation of specific physiological pain processes. However, what will be explored is the current knowledge of the relationship between obesity and cLBP, in addition to some of the potential mediating pathways. This research will include the distribution of body mass and its link to pain, as well as the experience of cLBP individuals in postural task performance.

Chapter 3: No Relationship Between Body Mass Index and Changes in Pain and Disability Following Exercise Rehabilitation for Patients with Mild to Moderate Chronic Low Back Pain

The text contained in this chapter was published in *Spine* in 2013.[197] Please note that aspects of the published article have required modification to conform to the chapter-style thesis format, including citation numbers, headings, and formatting of tables and figures. The mini abstract and key points included in the published article have been omitted.

3.1 Abstract

3.1.1 Study design

A retrospective, multi-centre study.

3.1.2 Objective

To investigate the relationship between BMI and changes in pain and disability resulting from exercise-based cLBP treatment.

3.1.3 Summary of background data

Past research has shown evidence of a relationship between BMI, a measurement of obesity, and cLBP. Exercise is a known beneficial treatment for cLBP. However, it is unclear if exercise-induced changes in pain and disability are related to baseline levels of, or changes in, BMI.

3.1.4 Methods

One hundred and twenty-eight (n=128) men and women with cLBP performed eight weeks of exercise, consisting of three to five exercise sessions (minimum of one supervised) per week. Outcome measures included BMI and self-reported pain and disability. BMI was calculated by weight divided by height squared (kg/m^2). Pain was measured using the Visual Analogue Scale (VAS) and disability was measured using the Oswestry Disability Index (ODI). Correlation, regression, covariance and likelihood ratios analyses were used to examine the relationship between BMI and self-reported pain and disability changes.

3.1.5 Results

No baseline relationships between BMI and self-reported pain (r=-0.083, p=0.349) and disability (r=0.090, p=0.314) were observed. There was no relationship observed between baseline BMI (r=0.938, p=0.873), or changes in BMI (r=0.402, p=0.854), with exercise-related changes in pain and disability respectively. No relationships between baseline BMI or BMI changes with pain and disability at baseline or following exercise were observed on the basis of pain and disability sub-groups. BMI was not a predictor of exercise-based pain and disability changes.

3.1.6 Conclusions

There was no significant relationship between BMI and self-reported pain and disability in cLBP participants. BMI was not a predictor of exercise-induced changes in pain and disability. The reliance on BMI as a sole measurement of obesity in cLBP research may be unwarranted.

3.1.7 Key words

Body mass index, chronic low back pain, self-reported pain and disability, exercise, obesity.

3.2 Introduction

cLBP is a widespread, disabling health condition[8, 10, 11] that affects 70-85% of people at some point in their life.[5, 154] In Australia, it is estimated that cLBP costs $9.17 billion dollars annually[13] as a result of treatment-related expenses and work absenteeism.[10, 13] cLBP refers to pain below the costal margin and above the gluteal fold, lasting for a minimum of 12 consecutive weeks.[4] Although the exact etiology of cLBP is unclear,[198] a possible relationship between obesity and cLBP has become evident.[6, 23, 78] For example, it has been suggested that obesity may affect pain and disability levels in cLBP[80] and can increase the risk of future cLBP development.[81]

Obesity is also a prevalent condition,[3, 14] with 20-25% of the Australian population reported as obese.[18] More importantly, obesity is common among low back pain sufferers.[76] Obesity is characterised by excess adipose tissue contributing to metabolic dysfunction.[2] A commonly used method to assess a person's degree of obesity is BMI,[3, 14] which is a known predictor of morbidity and mortality[3, 77] that is widely accepted and easily measured. BMI is a measure calculated from weight divided by height squared (weight/height^2).[3] Classification categories for BMI include <18.5kg/m^2 as underweight, 18.5-24.9kg/m^2 normal weight, 25.0-29.9kg/m^2 overweight, and ≥30.0kg/m^2 obese.[3, 78] BMI has been criticised by its inability to discriminate between fat and fat-free mass within the body, leading to possible misclassification.[73, 80] Regardless of such limitations, a relationship between BMI and cLBP has been identified.[23, 81]

BMI has not only been included as an obesity measurement in cLBP research, but has been used as a sole outcome measure.[23, 81] Research on the relationship between BMI and cLBP has produced conflicting results. For example, 21 of 65 included studies in a systematic review (32%) found a

significant weak but positive association between BMI or body weight and low back pain.[75] The remaining 44 studies did not find this significant positive association, or did not report on such an association.[75] Despite such inconsistent findings and lack of conclusive evidence for a definite link between BMI and cLBP, the regular use of BMI in cLBP research make it important for this relationship to be explored. More specifically, no studies have investigated the BMI-cLBP relationship with respect to pain and disability changes following a known treatment intervention, such as exercise. This is of importance, since exercise is a first-choice treatment for patients with cLBP.[85, 86]

Recent findings suggest that exercise may moderate the relationship between obesity and cLBP. For example, while overweight and obesity increase the risk of cLBP,[80] obese men and women exercising for one or more hours per week had 20% lower risk of cLBP than those that were inactive.[78] It remains unknown if BMI is associated with changes in pain and disability following exercise interventions for cLBP. Since BMI has been consistently used in cLBP research and shown to be associated with cLBP at baseline,[74, 80] it is important to explore this relationship over an intervention using exercise as the known beneficial treatment for cLBP. If BMI is unrelated to or an unsuccessful predictor of changes in cLBP, it may be concluded that the measurement has little value in cLBP research and the reliance on BMI alone is unjustified. Therefore the aim of this study was to investigate the relationship between BMI and exercise-induced changes in pain and disability in patients with cLBP.

3.3 Methods

3.3.1 Study design

This was a retrospective, multi-centre study of patients who underwent 8-weeks of exercise-based treatment for cLBP.

3.3.2 Patients

One hundred and twenty eight (n=128; Table 3.1) patients from randomised controlled trials conducted at two rehabilitation clinics in Western Sydney, Australia, between 2011 and 2013 were included in the study. Patients were recruited through media and email advertising, letterbox drops and local leaflet distribution. Inclusion criteria were men and women aged 18 to 55 years with cLBP below the costal margin and above the gluteal fold lasting for a minimum of 12 consecutive weeks. Exclusion criteria were history of spinal surgery, diagnosed lumbar disc herniation or fracture, existing cardiac or nervous system condition, diagnosed mental illness, severe postural abnormality, pain radiating below the knee, diagnosed inflammatory joint disease or recent (<3 months) therapeutic treatment (eg. manipulation, mobilisation).

Table 3.1 Patient Demographics and Measurement Outcomes at Baseline (n=128)	
Age (y)	36.47 ± 7.73
Height (m)	1.71 ± 0.09
Weight (kg)	81.70 ± 15.40
cLBP duration (y)	9.60 ± 7.14
BMI (kg/m^2)	27.82 ± 4.58
VAS current pain (/100)	39.5 ± 22.7
ODI score (%)	23.65 ± 11.68
Pain subgroups	
VAS: 0-44 (mm)	74
VAS: 45-100 (mm)	54
Disability subgroups	
ODI: 0-20 (%)	59
ODI >20 (%)	69
PrExType	
Core stability	81
Aerobic	47

Data presented as mean±SD
cLBP, chronic low back pain; BMI, body mass index; VAS, visual analogue scale; ODI, oswestry disability index; PrExType, predominant exercise type

3.3.3 Procedures

All patients were assessed for outcome measurements prior to and immediately after the exercise treatment program by blinded research assistants. Patients completed an 8-week exercise intervention after baseline assessment. The specific mode of exercise differed among patients, whereby 8 weeks of predominantly general aerobic exercise (eg. indoor stationary cycling) or predominantly core stability exercise (eg. trunk focused strength exercises and skilled contraction techniques) were performed. Three to five 1-hour exercise sessions (minimum of one supervised) per week of low-moderate intensity was required of all patients. Written informed consent was provided by patients prior to commencing the baseline assessment.

3.3.4 Outcome measurements

Height and weight were measured using standardised procedures and calibrated equipment. Patients wore lightweight clothing with their shoes off. Weight was measured to the nearest 0.1kg and height to the nearest 0.1cm. BMI was calculated by dividing the patient's weight by their height squared [weight(kg)/height(m)^2].[3] Self-reported current cLBP intensity was measured with a 100mm VAS,[49, 53] with the left anchor as "no pain" and the right anchor as "worst pain imaginable".[86, 199] Self-reported disability was measured with the ODI, a 10-item questionnaire resulting in a score out of 50 converted to a percentage[49, 51, 53] The VAS and ODI are valid and reliable methods of measuring pain and disability in cLBP.[199, 200]

3.3.5 Statistical analysis

SPSS v20.0 (IBM Corp., 2011) was used for statistical analysis. Normal distribution of data was assessed using Kolmogorov-Smirnov and Shapiro-Wilk tests of normality, in addition to tests of skewness and kurtosis. Baseline BMI, VAS and ODI did not show major deviations from normal distribution, so the relationship between baseline BMI with self-reported pain and disability, as measured by VAS and ODI respectively, was explored using Pearson correlation coefficients. Multiple linear regression analyses were applied to examine the relationship between baseline BMI and changes in BMI with percentage changes in VAS and ODI (((post–baseline)/baseline)x100) resulting from exercise. The dependent variable was VAS or ODI percentage change and the independent variable was baseline BMI or changes in BMI, with covariates of predominant exercise type (general aerobic, core stability), cLBP duration, age and average number of exercise sessions per week.

A secondary analysis was performed to investigate the effect of baseline pain and disability levels on the primary regression analysis. This consisted of multiple linear regression analyses on separate pain or disability subgroups using baseline VAS and ODI scores respectively. The subgroups included no pain to mild pain (VAS:0-44mm), moderate to severe pain (VAS:45-100mm),[201] no disability to minimal disability (ODI:0-20%), moderate disability (ODI:21-40%), severe disability (ODI:41-60%), crippling disability (ODI:61-80%) and bed-bound disability (ODI:81-100%).[202-204] The dependent and independent variables and covariates were consistent with the primary regression analysis.

While predominant exercise type was used as a covariate in all regression models, an analysis of covariance was performed to investigate the effect of predominant exercise modality (general aerobic or core stability) on BMI change. BMI change was the dependent variable, predominant exercise type was the between-subjects factor and average number of exercise sessions per week and baseline BMI were covariates. A final analysis was performed to examine whether clinically meaningful reductions (≥30% from baseline)[205] in VAS or ODI could be predicted by baseline BMI. Likelihood ratios were used to determine if VAS and ODI changes were successfully predicted by baseline BMI. Cut-off values for BMI were established from commonly used ranges for overweight (25.0-29.9kg/m^2) and obesity (≥30.0kg/m^2).[3, 78] Sensitivity (Sn), specificity (Sp) and likelihood ratios were then calculated, as described elsewhere,[206] for clinically meaningful reductions in VAS and ODI with respect to BMI cut-offs. Sn and Sp values closer to 1 indicated a greater likelihood of a true positive or a true negative occurrence.[207] Positive likelihood ratios (LR+) and negative likelihood ratios (LR-) above 10 and below 0.1 respectively indicated strong evidence to rule in or rule out a diagnosis.[206, 208] Mean and SD were calculated for continuous variables. Only data collected at outcome assessments was included in statistical analysis. The significance level was set to $p<0.05$.

3.4 Results

A total of n=128 patients were included in the study. Baseline outcome measurements are presented in Table 3.1. 54.7% (n=70) of patients had a BMI=25.0-29.9 and 22.7% (n=29) had a BMI≥30.0 at baseline. On the basis of pain sub-groups, n=74 patients reported a level of VAS=0-44mm and n=54 patients reported a baseline pain level of VAS:45-100mm. On the basis of disability sub-groups, n=59 patients reported a disability score of ODI:0-20% at baseline, n=59 reported a score of ODI:21-40% and a further n=8, n=2 and n=0 reported scores of ODI:41-60%, ODI:61-80% and ODI:81-100% respectively. Due to the small number of patients that reported baseline ODI>40%, the ODI:41-60%, ODI:61-80% and ODI:81-100% sub-groups were combined with the ODI:21-40% to form an ODI>20% sub-group of n=69 patients for analysis. Clinically meaningful reductions (≥30%)[205] in VAS and ODI after exercise were experienced by 57.8% (n=74) and 46.9% (n=60) of patients respectively.

3.4.1 Relationship between body mass index and self-reported pain and disability

There were no significant correlations observed between baseline BMI and baseline VAS (r=-0.083, p=0.349) or baseline ODI (r=0.090, p=0.314). Baseline BMI was not related to changes in VAS (β=-0.007, p=0.938) or ODI (β=0.015, p=0.873). Changes in BMI were also unrelated to changes in VAS (β=-0.077, p=0.402) or ODI (β=-0.017, p=0.854).

Results of the secondary analysis showed no evidence of baseline relationships between BMI and VAS (r=-0.116, p=0.325; r=0.066, p=0.638) or ODI (r=0.092, p=0.436; r=0.160, p=0.247) when sub-grouped by VAS:0-44mm and VAS:45-100mm respectively. Similarly, baseline BMI was not related to changes in VAS (β=0.007, p=0.956; β=-0.097, p=0.493) or ODI (β=0.120, p=0.337; β=-0.083, p=0.560) when

sub-grouped by VAS:0-44mm and VAS:45-100mm respectively. Changes in BMI were also unrelated to changes in VAS (β=-0.111, *p*=0.373; β=0.014, *p*=0.922) or ODI (β=0.005, *p*=0.969; β=-0.032, *p*=0.822) when sub-grouped in the same manner.

There were no baseline relationships found between BMI and VAS (*r*=-0.100, *p*=0.450; *r*=-0.146, *p*=0.230) or ODI (*r*=0.077, *p*=0.561; *r*=0.040, *p*=0.742) when sub-grouped by ODI:0-20% and ODI>20% respectively. Baseline BMI was not found to be related to changes in VAS (β=-0.085, *p*=0.578; β=0.042, *p*=0.730) or ODI (β=-0.091, *p*=0.536; β=0.118, *p*=0.335) when sub-grouped in the same manner. Changes in BMI were also unrelated to changes in VAS (β=-0.042, *p*=0.769; β=-0.097, *p*=0.433) or ODI (β=-0.098, *p*=0.484; β=-0.002, *p*=0.988) when sub-grouped by ODI:0-20% and ODI>20% respectively. Analysis of covariance showed that there was no significant effect of predominant exercise type on changes in BMI (*p*=0.459, 95%CI (-0.104, 0.228)).

Prediction categorisation analyses based on clinically meaningful reductions (≥30%) in VAS and ODI with respect to baseline BMI are presented in Table 3.2 and Table 3.3 respectively. LR+ ranged from 0.73 to 1.29 and 0.70 to 1.48 for VAS and ODI respectively, and LR- ranged from 0.73 to 1.09 and 0.63 to 1.11 for VAS and ODI respectively.

Table 3.2 Prediction categorisation of clinically meaningful reductions in VAS on the basis of BMI

BMI cut-off	Sn	Sp	LR+	LR-
≥25.0	0.63	0.51	1.29	0.73
≥30.0	0.19	0.74	0.73	1.09

VAS, visual analogue scale; BMI, body mass index; Sn, sensitivity; Sp, specificity; LR+, positive likelihood ratio; LR-, negative likelihood ratio

Table 3.3 Prediction categorisation of clinically meaningful reductions in ODI on the basis of BMI

BMI cut-off	Sn	Sp	LR+	LR-
≥25.0	0.65	0.56	1.48	0.63
≥30.0	0.19	0.73	0.70	1.11

ODI, oswestry disability index; BMI, body mass index; Sn, sensitivity; Sp, specificity; LR+, positive likelihood ratio; LR-, negative likelihood ratio

3.5 Discussion

This is the first study to investigate the relationship between BMI and exercise-induced changes in self-reported pain and disability in cLBP patients. Although 77% of the patients were classified as overweight or obese, there was no evidence of a baseline relationship between BMI and pain or disability. No relationship was found between baseline BMI and changes in pain and disability following exercise. Moreover, changes in BMI were not related to exercise-induced pain and disability changes. It was also shown that baseline BMI did not predict clinically meaningful reductions in self-reported pain and disability, despite 57.8% and 46.9% of patients experiencing such reductions in pain and disability respectively. The findings further showed that the likelihood of changes in pain and disability after exercise was not modified by BMI. The largest LR+ value was 1.20 and LR- was 0.53, indicating only minimal effects on the probability of a clinically meaningful reduction in pain or disability, since ratios above 10 and below 0.1 are strong evidence to rule in or rule out a diagnosis respectively.[206, 208] Based on the low-moderate Sn and Sp produced, the accuracy of the likelihood ratio results may be low. In addition, the lack of consideration for cut-off values in Sn and Sp analysis may have consequences associated with the incidence of false positive or false negative results, as was evident in the disparity of Sn and Sp values between a cut-off of BMI=25.0-29.9kg/m^2 in comparison to BMI>30.0kg/m^2. However, this is of little consequence since the overall modification of likelihood observed from LR+ and LR- was minimal. Consequently, these findings indicate that BMI alone may be of limited use as a predictor of pain and disability changes in cLBP.

In consideration of these results, criticism of the BMI measurement in the past[73, 80] may be valid. It could be suggested that BMI has been relied on too heavily in previous cLBP research and such reliance is unwarranted. Regardless of the evidence of a relationship between obesity and cLBP observed in earlier studies,[76] the findings of this study and the inconsistencies of past research[75] may

indicate that the use of BMI in cLBP research as a sole measure is not justified. The shift in research focus from obesity as a general concept to adipose tissue, in particular the distribution of adipose tissue, is further indication of the limitations of BMI as an obesity measurement. For example, adiposity has been linked to cLBP[12,42] and may be significant in the pathogenesis of pain.[80, 91-93] Consequently, simplistic measurements of obesity such as BMI are seemingly inadequate and of little relevance to cLBP. No studies have yet examined the relationship between alternative obesity and adiposity measures, such as ultrasound-derived subcutaneous and visceral abdominal adipose tissue thickness, with pain and disability in cLBP patients.

The results of this study suggest that exercise modality and the concomitant metabolic expenditure associated with each mode had no effect on BMI change, or the relationship between BMI change with pain and disability. It is possible that the 8-week exercise duration used in this study may not be sufficient to elicit BMI changes, since a dose-response relationship between exercise quantity and degree of weight loss has been previously suggested.[209] Exercise dose has not been investigated in cLBP, and a greater frequency of sessions or duration of intervention may produce different results pertaining to the BMI-cLBP relationship. However, consensus on exercise recommendations for inducing weight loss is lacking.[30] Moreover, nutritional intervention may be of greater importance than the total exercise dose for inducing weight loss, as caloric restriction in combination with exercise is said to be more effective than exercise alone.[31, 210] It must be considered that the exercise dose accrued in this study was sufficient to induce clinically meaningful reductions in pain and disability in 57.8% and 46.9% of patients respectively. The lack of an exercise modality effect on the relationship between BMI change with pain and disability suggests that research into a greater dose of exercise to elicit a BMI change may be of little relevance.

Due to the mild to moderate baseline level of pain and disability observed, the generalisability of findings may be limited to cLBP patients of the same pain or disability level. While possible that patients with increased pain or disability may have resulted in a relationship between BMI and cLBP, the generalisability of this study is strengthened by the sub-grouping analysis. The specific context of the study may also be a strength that previous research has lacked. For example, the 65 included studies of the aforementioned review included various body weight indices and an array of low back pain etiologies and definitions, ranging from acute to chronic conditions.[75] Irrespective of the possible reduced generalisability, this study's findings suggest that BMI is unrelated to cLBP, either at baseline or following an exercise intervention.

3.6 Conclusion

BMI was not found to be related to changes in pain and disability in cLBP patients following eight weeks of exercise. Examination of likelihood ratios suggested that BMI is not a successful predictor of clinically meaningful reductions in pain and disability in cLBP. For this reason, the reliance on the BMI measurement of obesity in cLBP research may be unwarranted. Future research into cLBP should focus on alternative measurements of obesity to BMI.

Chapter 4: Relative Abdominal Adiposity is Associated with Chronic Low Back Pain: a Preliminary Explorative Study

The text contained in this chapter was published in *BMC Public Health* in 2016.[211] Please note that aspects of the published article have required modification to conform to the chapter-style thesis format, including citation numbers, headings, and formatting of tables and figures.

4.1 Abstract

4.1.1 Background

Although previous research suggests a relationship between cLBP and adiposity, this relationship is poorly understood. No research has explored the relationship between abdominal-specific subcutaneous and visceral adiposity with pain and disability in cLBP individuals. The aim of this study therefore was to examine the relationship of regional and total body adiposity to pain and disability in cLBP individuals.

4.1.2 Methods

A preliminary explorative study design of seventy (n=70) adult men and women with cLBP was employed. Anthropometric and adiposity measures were collected, including body mass index, waist-to-hip ratio, total body adiposity and specific ultrasound-based abdominal adiposity measurements. Self-reported pain and disability were measured using VAS and ODI questionnaires respectively. Relationships between anthropometric and adiposity measures with pain and disability were assessed using correlation and regression analyses.

4.1.3 Results

Significant correlations between abdominal to lumbar adiposity ratio (A-L) variables and the WHR with self-reported pain were observed. A-L variables were found to predict pain, with 9.1-30.5% of the variance in pain across the three analysis models explained by these variables. No relationships between anthropometric or adiposity variables to self-reported disability were identified.

4.1.4 Conclusions

The findings of this study indicated that regional distribution of adiposity via the A-L is associated with cLBP, providing a rationale for future research on adiposity and cLBP.

4.1.5 Keywords

Chronic low back pain, obesity, abdominal adiposity, ultrasound, pain, disability

4.2 Background

cLBP places a large economic burden on society, with loss of income and treatment costs in Australia in excess of $9 billion annually.[13] LBP affects 10% of the global population and is ranked as the 7th leading disability in the world and the highest ranked for years lived with the disability.[26] Obesity is also a costly and prevalent health condition, which has been previously linked to cLBP.[23, 71-80] In the past this relationship has been demonstrated using BMI as a measure of obesity,[71, 74, 76, 78, 139] which has been defined as an individual's body weight divided by their height squared.[3] Despite its common use, the simplicity of BMI and its disregard for body composition[80] have led to its criticism and greater emphasis on alternative obesity measurements. This shift in focus is important because research suggests that adipose tissue may be of consequence in the pathogenesis of chronic pain conditions.[80] For example, increased adiposity (total body, upper and lower limbs, trunk, android and gynoid) is associated with higher levels of LBP intensity and disability.[80] US may be a suitable substitute for BMI and other simplistic obesity measurements as it is a valid and reliable measurement tool of assessing adiposity when compared to gold standard methods.[32, 90, 182-184, 186] However, US has not yet been utilized in cLBP research.

Although there is an established relationship between adiposity and LBP,[80] the inconsistent and poorly defined terminology used in the past makes previous research confusing and difficult to draw conclusions from. Moreover, there is a lack of research on the distribution of adiposity and its possible relationship with pain and disability levels in cLBP. No studies have investigated whether regionally accumulated abdominal adiposity may be of more relevance than total body adiposity in a cLBP population. For example, visceral adiposity has been suggested to be more important than total adiposity in the risk of developing obesity-related disorders.[89, 90] Visceral adiposity has also been suggested to be of greater consequence to the metabolic profile[32, 195] and various medical

pathologies[88] than subcutaneous adipose tissue, on the basis of physiological and metabolic differences such as adipocyte size and lipolytic activity.[196] It may then be suggested that the distribution of excess visceral adipose tissue could also be associated with increased pain in cLBP individuals. Several plausible mechanisms for a cLBP-visceral adiposity relationship exist, including inflammatory processes occurring from adipose tissue or increased mechanical load on the lumbar spine and surrounding structures produced by excess adiposity.[80] However, the cLBP-obesity relationship remains largely unknown, since research on the relationship between adiposity, primarily visceral, and cLBP is lacking.

In the exploration of the relative importance of regional versus total body adiposity, it is reasonable to believe that greater accumulation of adipose tissue in the abdominal region when compared to the lumbar region may also be of significance in the relationship to pain and disability in cLBP. This abdominal to lumbar adiposity ratio may be important, as greater abdominal adiposity could have flow-on effects for cLBP sufferers beyond that of an increase in body weight. For example, increased abdominal adipose tissue may result in the adoption of a compensatory hyperlordotic posture to counteract the constant anterior flexion torque placed on the lumbar spine. This excess anterior mass is worthy of investigation, as such an increase in compressive force may predispose the spine to injury.[163] Irrespective of the potential metabolic or biomechanical mechanisms that may be responsible for such a relationship, the parameters of a possible association between adiposity and cLBP should first be examined.

As a result of the inconsistencies of previous research and the potentially important consequences of visceral adiposity on the persistence of cLBP via metabolic factors such as the stimulation of inflammatory processes, it is warranted to examine the significance of adiposity distribution and particularly visceral adiposity on the obesity-cLBP relationship. US may then be employed to

investigate the possible importance of visceral adipose tissue, since it has been shown to be a valid and reliable method of assessing abdominal adiposity.[32, 90, 182-184, 186] Therefore, the aim of this study was to examine the relationship between regional and total body adiposity with pain and disability in cLBP individuals. The experimental objectives of this study were: 1) To use US-derived ratios to assess abdominal adipose tissue distribution in individuals with cLBP, 2) To perform correlation and regression analyses to examine relationships between anthropometric and adiposity variables with self-reported pain and disability in cLBP individuals, and 3) To perform the correlation and regression analyses on pain and disability subgroups within the cLBP dataset. The hypothesis of this study was that greater abdominal adiposity, particularly visceral, would be associated with increased self-reported pain and disability in a cLBP population.

4.3 Methods

4.3.1 Study design

A preliminary explorative study design was employed to examine the relationship between adiposity distribution with pain and disability in a cLBP population. All participant data was collected at a tertiary education facility in Western Sydney, Australia, over a three-year period with two cycles of participant recruitment and data collection.

4.3.2 Study population

Seventy (n=70) adult men and women aged 18-76 years were included in the study and were recruited through the use of media advertising and leaflet drops in the local area. All included participants had cLBP (pain between the costal margin and gluteal fold for a minimum of three months). Participants were excluded if they had a history of spinal surgery, spinal fracture, diagnosed lumbar disc herniation (and attained a positive result on the straight leg raise test), existing bone, cardiac or nervous system condition, diagnosed severe mental illness, severe postural abnormality, pain radiating below the knee or diagnosed inflammatory joint disease. Written informed consent was provided by all participants. This study had ethical approval for research on human subjects by the Human Research Ethics Committee review board on the basis of the Declaration of Helsinki.

4.3.3 Anthropometric measures

Height, weight, WC and hip circumference were measured while participants were barefoot and wearing lightweight clothing. Height was measured using a wall-mounted stadiometer (Veeder-Root high speed counter, Elizabethtown, N.C.) and recorded to the nearest 0.1cm. Weight was measured using a calibrated digital scale (A&D UC-321, A&D Co., Ltd) and recorded to the nearest 0.1kg. Waist circumference was measured using an anthropometric tape measure (Lufkin Executive Diameter Pocket Tape W606PM) at the narrowest point between the costal margin and the iliac crest and recorded to the nearest 0.1cm. Hip circumference was measured at the widest point of buttocks approximately level with the greater trochanters of the femur and recorded to the nearest 0.1cm. BMI and WHR were then calculated as weight divided by height squared $(kg/m^2)^3$ and WC divided by hip circumference, respectively.

4.3.4 Adiposity measures

4.3.4.1 Total body adiposity

Total body adiposity was measured using BIA (Metagenics VLA50, variation of ImpDF50, ImpediMed Limited, Eight Mile Plains, QLD, 2005), which has been shown to be a valid and reliable method when compared to gold standard methods.[33-36, 173, 176, 178, 179] Participants were required to refrain from food, drink and exercise 2 hours prior to the test and avoid alcohol in the 12 hours prior. Immediately prior to the test, participants emptied their bladder and lay supine on a plinth for 5 minutes to stabilise body fluids. The participant remained in this position with arms by their sides for the duration of the test. Pairs of electrodes (Ag/AgCl 3cm diameter, Kendall Medi-Trace 100, Tyco Healthcare Group LP, Mansfield, MA) were placed on their hand and foot on the right side of the body. Prior to electrode placement, the skin was adequately prepared using a safety razor, fine abrasion tape and alcohol

swabs to remove excess hair and reduce impedance. The hand electrodes were placed between the radial and ulna styloid processes 1cm proximal to the metacarpophalangeal joint of the middle finger. The foot electrodes were placed between the medial and lateral malleoli of the tibia and fibula, respectively, and 1cm proximal to the metatarsophalangeal joint of the middle toe. Each electrode pair was a minimum of 10cm apart. Resistance and reactance was recorded from the BIA device and then used to calculate total body adiposity percentage from the BIA software.

4.3.4.2 Regional adiposity

Regional adiposity (including lumbar, supra-iliac and multiple abdominal sites) was measured with US using previously validated and reliable methods.[32] Five subcutaneous adiposity and two visceral adiposity measurements were conducted over six anatomical locations on the surface of the skin in the trunk region of each participant, of which five have been described elsewhere.[32] Details and images of each measurement are listed in Table 4.1 and shown in Figures 4.1 and 4.2 respectively. Participants were required to lie supine for a period of 10 minutes prior to US testing to allow body fluids to stabilise. Each measurement required the use of conductive gel to gain a clear image.

Table 4.1 Ultrasound measurements			
Measurement	**Probe**	**Anatomical location**	**Method used for measurement**
msA	Linear	Just below the xiphoid process of the sternum	Minimum distance between the fat-skin barrier and the anterior surface of the linea alba
MppA	Linear	Just below the surface of the xiphoid process of the sternum (same anatomical position as the minimum subcutaneous adiposity measurement)	Maximum distance between the posterior surface of the linea alba and the anterior surface of the peritoneum covering the liver
MsA	Linear	(A) 2cm above the umbilicus and (B) 2cm below the umbilicus	Maximum distance in the centre of the image between the fat-skin barrier and the anterior surface of the linea alba
MiA	Convex	2cm above the umbilicus (same anatomical position as the maximum subcutaneous abdominal adiposity A measurement)	Maximum distance in the centre of the image between the posterior surface of the rectus abdominis muscle and the anterior wall of the abdominal aorta
MsSI	Linear	Just above the iliac crest on the mid-axillary line	Maximum distance between the fat-skin barrier and the anterior surface of the external oblique muscle
MsL	Linear	Level of L4/L5 directly over the lumbar erector spinae muscle	Maximum distance between the fat-skin barrier and the anterior surface of the lumbar erector spinae muscle
msA, minimum subcutaneous abdominal adiposity; MppA, maximum pre-peritoneal abdominal adiposity; MsA, maximum subcutaneous abdominal adiposity; MiA, maximum intra-abdominal adiposity; MsSI, maximum subcutaneous supra-iliac adiposity; MsL, maximum subcutaneous lumbar adiposity			

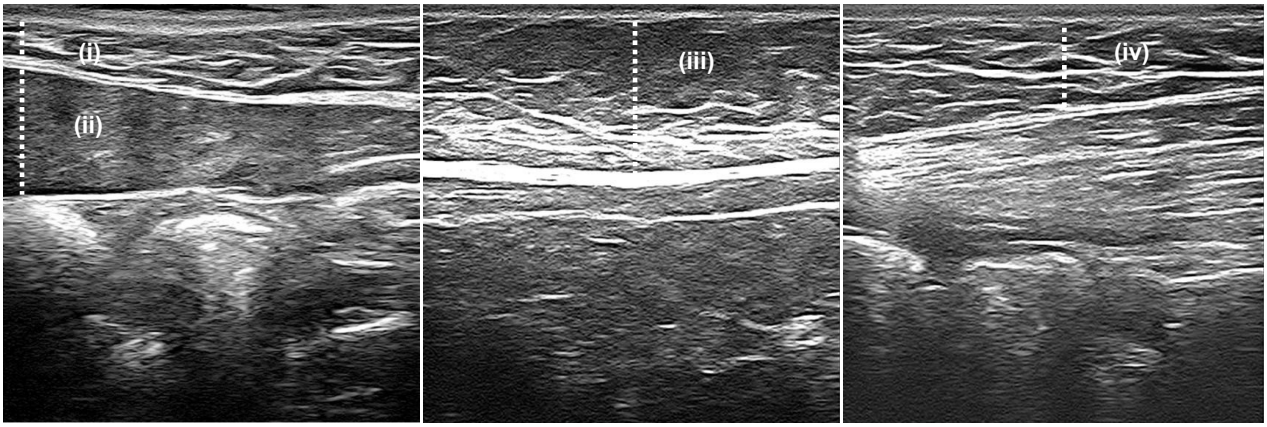

Figure 4.1 Examples of abdominal US measurements (i) minimum subcutaneous abdominal adiposity (ii) maximum pre-peritoneal abdominal adiposity (iii) maximum subcutaneous abdominal adiposity A (iv) maximum subcutaneous abdominal adiposity B

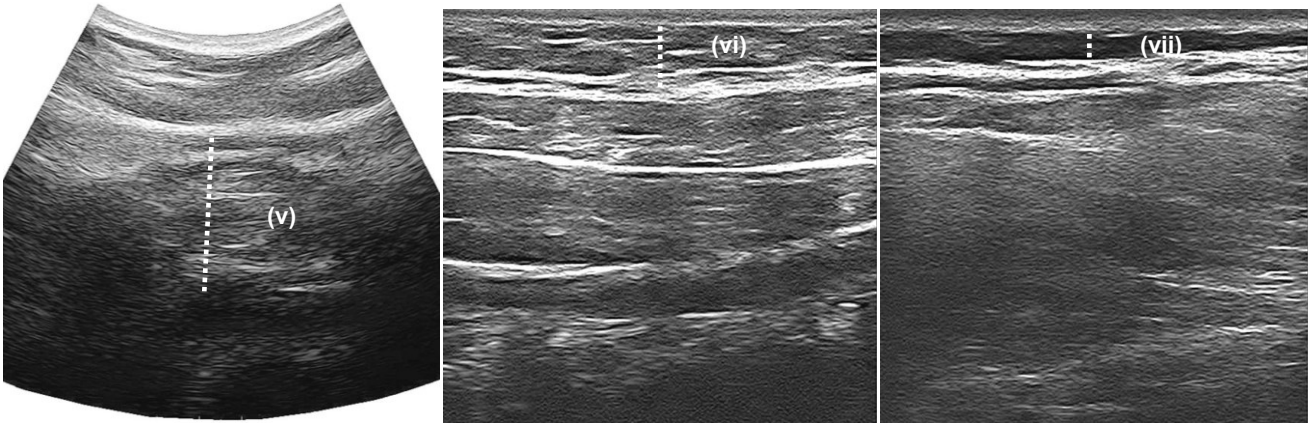

Figure 4.2 Examples of intra-abdominal, supra-iliac and lumbar US measurements (v) maximum intra-abdominal adiposity (vi) maximum subcutaneous supra-iliac adiposity (vii) maximum subcutaneous lumbar adiposity

4.3.4.3 Adiposity ratios

The adiposity ratios calculated from ultrasound-derived adiposity thickness measurements are defined in Table 4.2, of which one has been previously described.[32] Such ratios were worthy of inclusion as past research has questioned simplistic anthropometric measurements such as BMI and WHR due to their lack of sensitivity and specificity.[80, 212, 213] Additionally, existing evidence implies a relationship between adiposity and pain that may be complex and multifactorial.[80] Consequently, the examination of adiposity relative to the individual may be crucial to better understanding the relationship between adiposity and cLBP.

Table 4.2 Ultrasound-derived adiposity variables

Measure	Calculation	Definition
A-L	(MsAa + MiA) / MsL	Abdominal-to-lumbar adiposity ratio (subcut. + visc. abdo measures for total abdominal adiposity thickness relative to lumbar adiposity thickness)
S-M	(MsAa + MsSI + MsL) / weight	Subcutaneous adiposity to mass ratio (total subcutaneous trunk adiposity thickness relative to overall body mass)
V-M	(MppA + MiA) / weight	Visceral adiposity to mass ratio (total visceral trunk adiposity thickness relative to overall body mass)
MAR-A	MsAa / MiA	Maximal abdominal ratio A (ratio between subcutaneous and visceral abdominal adiposity)
A-L/BMI	[(MsAa + MiA) / MsL] / [weight / (height x height)]	Abdominal-to-lumbar adiposity ratio relative to BMI (ratio between abdominal and lumbar adiposity thickness relative to overall body mass index
A-L/WHR	[(MsAa + MiA) / MsL] / (waist circumference / hip circumference)	Abdominal-to-lumbar adiposity ratio relative to WHR (ratio between abdominal and lumbar adiposity thickness relative to the ratio between waist and hip circumferences)
TC-TBF	(MsAa + MsSI + MsL) / total body adiposity percentage	Total circumference relative to total body adiposity ratio (total trunk circumference adiposity thickness relative to total body adiposity percentage)

MppA, maximum pre-peritoneal abdominal adiposity; MsAa, maximum subcutaneous abdominal adiposity A; MiA, maximum intra-abdominal adiposity; MsSI, maximum subcutaneous supra-iliac adiposity; MsL, maximum subcutaneous lumbar adiposity

4.3.5 Pain and disability

Self-reported pain was measured using a VAS, with 'no pain' on the left anchor and 'worst pain imaginable' on the right anchor, whereby the participant rated their current cLBP on a 100mm line.[199, 214] Self-reported disability was measured using the ODI questionnaire, whereby participants filled in a 10-item questionnaire that was scored and converted to a percentage.[86, 199, 214] VAS and ODI have been previously shown to be valid and reliable methods of measuring self-reported pain and disability respectively in pain research, including cLBP populations.[200, 203, 215-218]

4.3.6 Statistical analysis

Statistical analyses were performed using SPSSv23 (IBM Corp., 2015). Mean and standard deviation were presented for characteristics of the study sample. Normal distribution of data was assessed by Kolmogorov-Smirnoff and Shapiro-Wilk tests, and examination of Q-Q plots, frequency histograms and standard errors of skewness and kurtosis. Variables not normally distributed were log transformed and parametric methods of analysis were then used. Three (3) datasets were used for statistical analysis; the total sample of participants (n=70) to avoid the potential for detection bias, a VAS subgroup with a minimum level of pain as indicated by 2.0 or greater on the VAS scale (n=42), and an ODI subgroup with a minimum level of disability as indicated by 10.0% or greater on the ODI questionnaire (n=52). Pearson correlation coefficients were used to identify relationships between anthropometric and adiposity variables with self-reported pain and disability. Stepwise regression analyses were performed to explain relationships between anthropometric and adiposity variables with pain and disability, as well as determine the proportion of variance in pain and disability explained by such variables. Adjusted R square values were reported for significant relationships. Predictor variables included in the regression analysis were determined by the results of the correlation analysis, where only variables found to be correlated with pain or disability were included

in the regression models to reduce the potential effect of confounding variables. The variance inflation factor (VIF) was used to determine the effect of collinearity of prediction variables on regression analyses. A VIF>5 for any two variables was used to indicate collinearity, in which case the variable with the higher VIF was removed from the prediction model. Missing data were addressed through exclusion of the incomplete variable/s for a given participant from the analysis model. The study size was arrived at with the use of post-hoc calculations of statistical power. Statistical significance was set at $p<0.05$.

4.4 Results

A total of n=122 individuals were screened for inclusion and n=70 cLBP individuals were eligible and chose to participate in the study. The characteristics of the study sample are summarised in Tables 4.3-4.5. One participant had missing data of the minimum subcutaneous lumbar adiposity measurement.

Table 4.3 Demographic characteristics of the study sample (n=70)	
Age (yrs)	39.57 ± 11.01
cLBP (yrs)	9.84 ± 8.60
Gender (M/F)	30M, 40F
Height (m)	1.70 ± 0.08
Weight (kg)	79.66 ± 17.44
BMI (kg/m^2)	27.49 ± 5.63
WC (cm)	87.72 ± 14.68
HC (cm)	104.94 ± 10.03
WHR	0.83 ± 0.09
%TBF	29.99 ± 10.87
ODI	16.66 ± 9.65
VAS	2.38 ± 1.78
Data mean ± SD; cLBP, chronic low back pain; BMI, body mass index; WC, waist circumference; HC, hip circumference; WHR, waist-to-hip ratio; %TBF, total body adiposity percentage; ODI, oswestry disability index; VAS, visual analogue scale	

Table 4.4 Absolute ultrasound measurements (mm) of the study sample (n=70)	
msA	12.34 ± 7.79
MppA	13.36 ± 4.53
MsAa	20.19 ± 9.69
MsAb	19.60 ± 9.90
MiA	49.77 ± 23.01
MsSI	14.40 ± 7.69
MsL	8.36 ± 6.90
Data mean ± SD; msA, minimum subcutaneous abdominal adiposity ; MppA, maximum pre-peritoneal abdominal adiposity ; MsAa, maximum subcutaneous abdominal adiposity A; MsAb, maximum subcutaneous abdominal adiposity B; MiA, maximum intra-abdominal adiposity ; MsSI, maximum subcutaneous supra-iliac adiposity ; MsL, maximum subcutaneous lumbar adiposity	

Table 4.5 Relative ultrasound measurements and ratios of the study sample (n=70)	
A-L	12.42 ± 9.12
S-M	0.54 ± 0.24
V-M	0.78 ± 0.20
MAR-A	0.46 ± 0.25
A-L/BMI	0.47 ± 0.38
A-L/WHR	14.44 ± 10.11
TC-TBF	1.44 ± 0.52
Data mean ± SD; A-L, abdominal to lumbar adiposity ratio; S-M, subcutaneous adiposity to mass ratio; V-M, visceral adiposity to mass ratio; MAR-A, maximum abdominal ratio A; A-L/BMI, abdominal to lumbar adiposity ratio relative to BMI; A-L/WHR, abdominal to lumbar adiposity ratio relative to WHR; TC-TBF, total circumference relative to total body adiposity ratio	

4.4.1 Relationship between anthropometric and adiposity measures to pain and disability

Correlations between anthropometric and adiposity measures with pain are shown in Table 4.6. There were no significant correlations observed between self-reported disability and anthropometric or adiposity variables in any of the analysis models. ODI was found to be correlated to VAS in the total sample ($r=0.264$, $p=0.028$), but not in either of the subgroup analysis models.

Stepwise regression showed that 9.1% ($p=0.007$) of the variance in pain was explained by A-L alone in the total sample analysis ($n=70$), which was increased to 15.7% ($p=0.001$) when ODI was added to the model. Results of the stepwise regression for the VAS subgroup indicated that 30.5% of the variance in pain could be explained by A-L relative to WHR (A-L/WHR, $p<0.001$). Similar results were observed in the ODI subgroup regression analysis, as 24.7% of the variance in pain was explained by A-L relative to BMI (A-L/BMI, $p<0.001$). No regression analysis was performed on self-reported disability on the basis of no significant correlations to anthropometric or adiposity variables in any of the analysis models. Post-hoc results revealed an achieved statistical power of $\beta=0.75$ for the variance in pain explained by A-L/WHR.

Table 4.6 Significant correlations between anthropometric and adiposity variables with self-reported pain

Analysis model	Variable	*r*	*p*
Total sample (n=70)	A-L	0.323	0.007
	A-L/WHR	0.315	0.008
	A-L/BMI	0.303	0.011
VAS subgroup (n=42)	A-L	0.566	<0.001
	A-L/WHR	0.568	<0.001
	A-L/BMI	0.546	<0.001
ODI subgroup (n=52)	A-L	0.493	<0.001
	A-L/WHR	0.438	0.001
	A-L/BMI	0.5111	<0.001
	WHR	0.287	0.039

VAS, visual analogue scale; ODI, oswestry disability index; A-L, abdominal to lumbar adiposity ratio; A-L/WHR, abdominal to lumbar adiposity ratio relative to WHR; A-L/BMI, abdominal to lumbar adiposity ratio relative to BMI; WHR, waist-to-hip ratio

4.5 Discussion

It was hypothesised that greater abdominal adiposity, particularly visceral, would be associated with increased self-reported pain and disability in cLBP individuals. This study's findings showed a relationship between anthropometric and adiposity measures to self-reported pain in cLBP, but not disability. More specifically, A-L relative to the size of the individual was the best predictor of self-reported pain.

The results of this study support previous suggestions that visceral adiposity may be more important than subcutaneous adiposity in the relationship to pain. For example, the overflow of adipocytes into excess visceral and ectopic stores may initiate a process of metabolic dysfunction[91] resulting from the disrupted equilibrium between energy intake and lipid oxidation.[213] Consequently, this overflow may promote the release of adipocyte-derived pro-inflammatory cytokines[93] contributing to insulin resistance and end-stage disease,[91, 93] but also to hyperalgesia and central sensitisation.[92] In addition to metabolic dysfunction, there is growing evidence for the pathophysiological consequences on bone and skeletal muscle integrity and function from abnormal lipid accumulation.[213] The result may then be chronic low-grade systemic inflammation[91, 93] and therefore the persistence of a chronic pain state.[92] For example, increased levels of CRP, a sensitive acute-phase protein associated with body adiposity measures,[219] has been linked to greater odds of reporting LBP symptoms, particularly in those measured as obese by BMI or WC.[219] It has been suggested that increased CRP may be indicative of early signs of low-grade chronic systemic inflammation.[219] Consequently, it may validate the implication of pro-inflammatory cytokines in the complex pathways of musculoskeletal pain[219] and further support the use of visceral adiposity measurements, such as US, in the research of cLBP and other chronic pain pathologies.

This study's findings may also support a theorised metabolic mediation in the adiposity-pain relationship.[80] Since pain was found to be significantly correlated with A-L relative to BMI or WHR, visceral adiposity relative to body size and shape may be an important consideration for future research. For example, the distribution of A-L may be just as important as the overall representation of body size and mass distribution. Therefore, it may be the accumulation of body mass coupled with greater levels of relative adiposity that puts an individual in an increased or more persistent cLBP state.

The moderate to strong correlations and prediction models between pain and A-L relative to WHR and BMI may advocate a possible physiological or biomechanical mediation between obesity and cLBP. For instance, WHR measures an individual's anatomical circumference of the waist compared to the hips to assess adiposity distribution[220] and the associated risk of deviating from optimal body morphology for physical health. In turn, BMI is a measure of overall body size as a relative association between height and weight,[3] with an optimum balance to achieve the 'healthy' range. Consequently, coupling WHR and BMI with the A-L/pain relationship may further support a physiological or biomechanical mediation. It is reasonable to believe that the body can only manage a degree of anterior-to-posterior load, but is also functionally limited by waist-to-hip load and overall body load. For example, perhaps an individual with a high A-L, large WHR and elevated BMI may be in greater pain than someone with the same A-L but lower WHR and BMI. It may be the accumulation of the overall body mass and weight distribution including adiposity that acts as a pain catalyst, but is the A-L that is most instrumental in observable and measurable biomechanical changes. For instance, it is plausible that greater anterior mass may result in increased compensatory lordosis during normal daily posture, manifest by spinal hyperextension, and thereby excess abdominal adiposity may result in increased magnitude or repetition of compression loading, which is a known precursor for risk of intervertebral disc injury.[163] Moreover, previous research suggests that both vertebral joint

compression and postural deviation may impact upon shear injury potential.[164] Irrespective of these yet unconfirmed inferences, it is known that obesity and cLBP are linked[23, 71-80] and that simplistic measurements like BMI are unrelated to cLBP[197] and lack the sensitivity to detect excessive adiposity in non-obese individuals.[213] Therefore, future research may need to explore more comprehensive measurements such as A-L to further quantify and explain the adiposity-cLBP relationship.

The hypothesis that greater abdominal adiposity would be associated with increased disability was not supported, as no correlations were found between anthropometric and adiposity variables with disability. This finding was not supported or refuted by previous research, since no other studies to the authors' knowledge have examined the relationship between adiposity and disability associated with cLBP. An earlier study reporting a relationship between adiposity and disability associated with LBP[80] was not specific to cLBP and assessed adiposity and disability using different methods to those used in this study. Therefore, further research may be necessary to confirm that adiposity and disability are unrelated in cLBP.

The novelty of this research lends itself to potential constraints, such as the use of absolute and relative adiposity ratios not previously studied. The removal of variables to eliminate collinearity during statistical analysis may have excluded potentially relevant variables from the prediction models. However, any variables removed were those with the least impact on the prediction models. Correlation analysis between each variable with pain and disability also ensured all relevant relationships between variables were explored. It may be irrelevant which A-L variables were left in the regression analyses, since all A-L variables were found to have strong correlations to pain. The use of WHR instead of WC may be a limitation since adipose tissue deposits in the abdominal versus gluteofemoral region may have different biological mechanisms and therefore altered health risk implications.[220] For this reason, future studies into the A-L/cLBP relationship may benefit more from

the use of WC instead of WHR. The selection of VAS and ODI cutoff values may have excluded potentially relevant data, but since the majority of existing research explored the minimum level of clinically meaningful change over time no previous consensus on normative scores for minimal pain or disability levels in cLBP was found. Therefore, values were set from collaborative evidence of minimal important change values in VAS ranging from 1.5-2.0[205] and a normative score of 10.19 for ODI of 'normal' populations,[203] which was deemed appropriate based on available evidence. The study results can only be generalised to adult cLBP populations.

4.6 Conclusions

The results of this study demonstrated significant relationships between abdominal adiposity and cLBP. A-L combined with increased WHR and BMI was a predictor of pain variance. Therefore, an individual's adiposity distribution relative to their body or trunk mass may be of greater importance in the cLBP-obesity relationship than single measurements alone. These findings support the use of US-based methodologies for future cLBP research. Until the mechanisms responsible for the adiposity-cLBP relationship are better understood, attempts to manipulate it through pain or adiposity reduction treatment may be of little benefit. For this reason, additional research into possible physiological, metabolic and biomechanical mediators between adiposity distribution and pain manifestation in cLBP is warranted.

Chapter 5: What Explains Task Performance? An Exploration of Relationships Between Relative Abdominal Adiposity, Lumbar Muscle Endurance, Pain Development and Task-induced Lumbar Flexion in cLBP Individuals Performing the Biering-Sorensen Test

5.1 Introduction

The Biering-Sorensen test is a common postural task for assessing lumbar muscle endurance,[221] which requires an individual to hold their upper body in an unsupported horizontal position.[221-224] This position is maintained for a specified time period or until volitional exhaustion.[221, 225] It has been shown that people with cLBP exhibit shorter task duration times compared to healthy asymptomatic individuals.[221, 224] While mechanisms of fatigue and reasons for task failure during the Sorensen test have been previously studied,[224, 226, 227, 228, 229] past research lacks consideration of body mass distribution and its potential effect on task performance. Body mass distribution may be of relevance and importance to the Sorensen test, due to the possibility that abdominally-accumulated adiposity may contribute to pain provocation and consequently test cessation. For example, the mechanical load on the lumbar spine and surrounding structures (ligaments, tendons, muscles) from excess anterior mass[80] may increase back pain experienced and reported during the test, and lead to premature test cessation. This possibility is supported by the previous work of the author (see Chapter 4), which identified a relationship between anthropometric and adiposity measures to self-reported cLBP.[211] More importantly, an individual's A-L relative to the regional and overall size of the individual was found to be a significant predictor of pain.[211] It has been suggested that the human body may be restricted by certain tolerable levels of anterior-to-posterior loading, in addition to that of the overall body size and regional waist-to-hip load.[211] Moreover, deviations from this tolerated

loading may be observed through pain responses, whereby correlations between pain and relative A-L may indicate an underlying physiological or biomechanical mediation between adiposity and cLBP.[211] For instance, cLBP individuals with larger A-Ls may exhibit poorer Sorensen performance and greater pain development than those with lower A-Ls.

Moreover, Sorensen duration may be moderated by body mass distribution through its influence on spinal extensor muscle fatigue, which refers to the decline of a muscle or muscle group to generate force or power.[230] In the context of the Sorensen test, muscle fatigue indicates an inability of the lumbar muscles to continue producing sufficient force to maintain the required horizontal position. In cLBP populations, it has been suggested that they may adopt varying neuromuscular strategies, possibly moderating back extensor muscle fatigue.[231] If cLBP individuals are already at a predisposition to greater paraspinal fatigue as previous research suggests,[221, 227, 228, 232] it is plausible that those with increased A-Ls may exhibit shorter Sorensen duration than those with more favourable body morphology. Therefore, adipose tissue distribution such as the A-L may initiate a muscle recruitment strategy that explains Sorensen task performance. For example, a study on male construction workers found those with a definite low back disorder used a higher percentage of maximum trunk extensor strength during the test, compared to those with probable or no history of low back disorder.[233] Although it only accounted for 8% of the variability[233] and the study population was not clearly identified as having cLBP, it may suggest that people with LBP have increased lumbar muscle recruitment that predisposes them to more rapid fatigability. Therefore, it may be reasonable to believe that body mass distribution is the missing link to different neuromuscular strategies in cLBP.

Another consideration may be a link between paraspinal muscle fatigue and task-induced flexion of the lumbar spine. Previous studies have shown that lumbar flexion may coincide with LBP, reductions

in lumbar muscle endurance[94] and excessive activation of spinal extensor muscles leading to increased tissue strain.[95] Research suggests that those with a 'flexion pattern' pain disorder exhibit greater flexion and rotation of the lumbar spine compared to those without cLBP, as well as compensatory adjustments to trunk muscle contraction as a reflex pain response.[95] In a study on healthy individuals, a lower rate of paraspinal muscle fatigue and longer task duration times were observed in a modified version of the Sorensen test compared to the original.[231] The authors attributed the disparity to increased thoracolumbar fascia contribution, resulting from greater hip extensor muscle stretch in the modified test. However, they also raised the need for investigation of the potential relationship between lordotic curvature and paraspinal muscle fatigue.[231] It may be possible for increased abdominal adipose tissue to induce greater task-specific lordotic curvature (manifest by spinal flexion), which has been associated with the presence of LBP and reduced lower back muscle endurance.[94] This reduction in muscular endurance may result from the increased activation of lumbar muscles to compensate for the acute spinal movement. Such a theory is supported by the knowledge that activities largely involving the counteraction of gravity are associated with increased fatigability in people with obesity, due to greater force production requirements.[169] Additionally, research shows that BMI has a negative effect on lumbar paraspinal muscle fatigability in both genders, mainly at the L4-L5 level and particularly in women.[234] Since no studies have yet examined the effect of body mass distribution on Sorensen test performance in cLBP, such propositions are yet to be confirmed. One previous study on construction workers with and without LBP[233] measured the torque of trunk weight, which was calculated by the distance between the anterior superior iliac spine and the centre of the shoulder joint. They then explored the relationship to isometric trunk muscle endurance using the Sorensen test. No significant correlation between torque of trunk weight and endurance time was identified.[233] However, they did not control for body mass distribution between the two populations tested.

Previous research has established that obesity has negative consequences on muscle fatigue[169, 234] and that relative adiposity is related to cLBP,[211] yet no studies have explored the effect of adiposity distribution on the Sorensen test. Moreover, it remains unknown if body mass and adiposity distribution is associated with task performance, and if so whether this relationship can be explained by spinal movement or lumbar muscle fatigue. For this reason, the objective of this study was to examine relationships between relative abdominal adiposity, lumbar muscle endurance, self-reported pain development and lumbar spinal flexion with Sorensen test duration time in cLBP. It was hypothesised that increased body mass and abdominally-accumulated adiposity would be associated with shorter task duration times, and that this association would be explained by increased spinal flexion and faster rates of muscle fatigue.

5.2 Methods

5.2.1 Study design

A cross-sectional study was used to examine the effect of abdominal mass distribution on the Biering-Sorensen test in cLBP individuals. All data was collected in a university laboratory setting.

5.2.2 Participants

Fifty-two (n=52) adults with cLBP were included in the study. Participants were recruited through the use of local newspaper advertising and leaflet distribution. The study included men and women aged 18 to 55 years, with cLBP below the costal margin and above the gluteal fold lasting for a minimum of 12 consecutive weeks. Individuals were excluded from the study if they had undergone previous spinal surgery, had a diagnosed structural issue (eg. lumbar disc herniation), existing cardiac or nervous system condition, or a history of diagnosed mental illness (eg. depression). Written informed consent was received from all participants prior to testing. Ethical approval was granted by the University Human Research Ethics Committee on the basis of the Declaration of Helsinki.

5.2.3 Procedure

A single testing session was required for each participant in the study, in which anthropometric and adiposity outcome measures were assessed, including weight, BMI, WC, WHR, %TBF, and relative abdominal adiposity variables. Self-reported pain and disability were also recorded. Each participant then performed the Biering-Sorensen test of lumbar endurance.

5.2.3.1 Biering-Sorensen test

Each participant was required to lie prone on a plinth with the level of the superior border of the iliac crest at the edge of the plinth and their legs secured by straps, as used elsewhere.[221] The straps were placed around the lower portion of the gastrocnemius muscles and across the hamstrings inferior to the gluteal fold, with folded towels used under the ankles for improved comfort. During the test, individuals were required to keep their arms folded across their chest with their hands touching opposite shoulders and to maintain their upper body in an unsupported isometric horizontal position for 'as long as possible'. The participant's upper body position was monitored throughout the test and prompts were provided when necessary for position correction. Test termination criteria included an inability of the participant to continue to maintain the correct horizontal position for five consecutive seconds, or due to volitional exhaustion. Sorensen duration time was recorded by a stopwatch as the time from commencement to termination. Prior to the commencement of the test, participants were given a five-second practise hold for familiarisation.

5.2.4 Outcome measurements

5.2.4.1 Anthropometric measurements

Height, weight and WC were measured while participants were barefoot and wearing lightweight clothing. Height was measured with a wall-mounted Veeder-Root high speed counter stadiometer to the nearest 0.1cm. Weight was recorded from an A&D calibrated digital scale to the nearest 0.1kg. WC was measured at the narrowest point between the costal margin and the iliac crest[212] to the nearest 0.1cm. Hip circumference was measured at the widest point of the buttocks[212] approximately level with the greater trochanters of the femur, and was recorded to the nearest 0.1cm. BMI was calculated as weight divided by height squared (kg/m^2).[3] WHR was calculated as WC divided by hip circumference.[104]

5.2.4.2 Total body adiposity

%TBF was measured using an ImpediMed BIA system, shown to be valid and reliable compared to gold standard methods.[33-36, 173, 176, 178, 179] BIA required each participant to refrain from food, drink and exercise 2 hours prior to the test and avoid alcohol in the 12 hours prior. Immediately prior to commencement, participants were asked to empty their bladder and lay supine on a plinth for 5 minutes to stabilise body fluids. The participant remained in this position with arms by their sides for the duration of the test. The skin was adequately prepared to reduce impedance through excess hair removal, fine abrasion tape and alcohol swabs. Pairs of Ag/AgCl electrodes were then applied to the right hand and foot between the radial and ulna styloid processes of the wrist and 1cm proximal to the metacarpophalangeal joint of the middle finger; and between the medial and lateral malleoli of the tibia and fibula, and 1cm proximal to the metatarsophalangeal joint of the middle toe, respectively. Each electrode pair was a minimum of 10cm apart. Resistance and reactance was recorded from the BIA device and then used to calculate %TBF from the BIA software.

5.2.4.3 Relative abdominal adiposity

Abdominal adiposity was assessed using an Echowave II 2.3.6 LogicScan 128 EXT-1Z Series Beamformer ultrasound device involving linear measurements of adipose tissue thickness based on anatomical references such as the linear alba,[32, 182] and using previously validated and reliable methods.[32] Prior to US testing, participants were required to lie supine on a plinth for a period of 10 minutes to allow body fluids to stabilise and conductive gel was used to gain clear images. One visceral adiposity and three subcutaneous adiposity measurements were conducted over three anatomical locations on the surface of the skin in the trunk region of each participant, of which two have been described elsewhere.[32] Details of each measurement are shown in Table 5.1 and Figures 5.1 and 5.2 respectively. The following relative adiposity ratios were calculated from US-derived

adiposity thickness measurements: A-L, abdominal-to-lumbar adiposity; A-L/WC, abdominal-to-lumbar adiposity relative to waist circumference; and TC-TBF, total trunk adiposity circumference relative to percentage of total body adiposity. Given the nature of the Sorensen test and parameters being explored, such adiposity ratios were considered worthy of inclusion.

Table 5.1 Ultrasound measurements

Measurement	Probe	Anatomical location	Method used for measurement
MsAa	Linear	2cm above the umbilicus	Maximum distance in the centre of the image between the fat-skin barrier and the anterior surface of the linea alba
MiA	Convex	2cm above the umbilicus (same anatomical position as the maximum subcutaneous abdominal adiposity A measurement)	Maximum distance in the centre of the image between the posterior surface of the rectus abdominis muscle and the anterior wall of the abdominal aorta
MsSI	Linear	Just above the iliac crest on the mid-axillary line	Maximum distance between the fat-skin barrier and the anterior surface of the external oblique muscle
MsL	Linear	Level of L4/L5 directly over the lumbar erector spinae muscle	Maximum distance between the fat-skin barrier and the anterior surface of the lumbar erector spinae muscle

MsAa, maximum subcutaneous abdominal adiposity; MiA, maximum intra-abdominal adiposity; MsSI, maximum subcutaneous supra-iliac adiposity; MsL, maximum subcutaneous lumbar adiposity

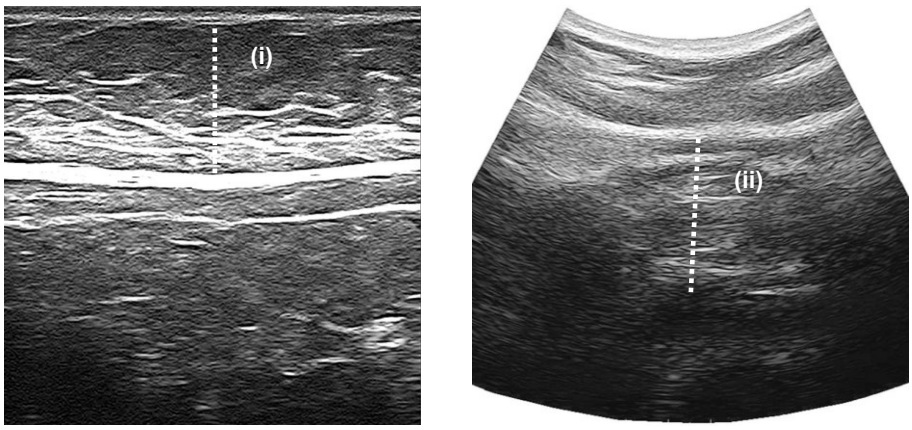

Figure 5.1 Examples of abdominal US measurements. (i) maximum subcutaneous abdominal adiposity A. (ii) maximum intra-abdominal adiposity.

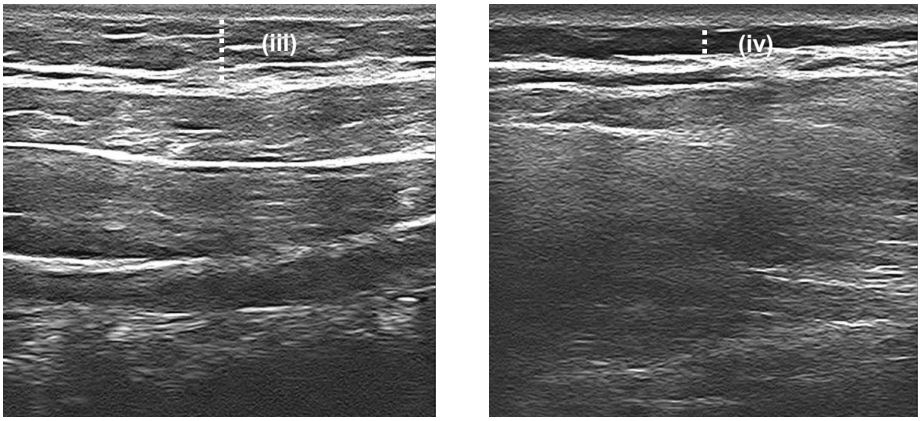

Figure 5.2 Examples of supra-iliac and lumbar US measurements. (iii) maximum subcutaneous supra-iliac adiposity. (iv) maximum subcutaneous lumbar adiposity.

5.2.4.4 Pain

Self-reported pain was measured using a VAS. Current levels of cLBP were recorded by the participant on a 100mm line, with 'no pain' on the left anchor and 'worst pain imaginable' on the right anchor.[199, 214] Participants were also asked to verbally rate their current level of lower back pain from one to ten prior to, every 20 seconds throughout and immediately after termination of the Sorensen test, using a larger VAS placed on the floor directly beneath them for reference. The VAS questionnaire has been

previously shown to be a valid and reliable method of measuring self-reported pain in cLBP and other pain research.[215-218]

5.2.4.5 Surface electromyography (sEMG)

Pairs of Ag/AgCl electrodes (Maxensor, MediMax Global, Australia) with a contact diameter of 10mm and center-to-center interelectrode distance of 10mm were placed on the surface of the skin, overlying the muscle fibres of the right and left lumbar erector spinae longissimus (LES) muscle approximately 2cm lateral to the spinous processes of the L4/L5 vertebrae. Electrodes were applied to the skin prior to testing and were placed in accordance with SENIAM guidelines via palpation of known bony landmarks to ensure consistency among study participants. Skin was carefully prepared prior to electrode placement to reduce impedance to below 5Ω, by the removal of excess hair with disposable razors, light skin abrasion using fine sandpaper and use of isopropyl alcohol swabs. Raw electromyographic (EMG) muscle signals were recorded continuously throughout the Sorensen test, using a biological amplifier system (common mode rejection ratio >85dB at 50Hz, input impedance 200MΩ; Powerlab, AD Instruments, Australia) sampled at 2000Hz with a 16-bit analog to digital conversion. An initial fourth-order Bessel filter between 20 and 500Hz was applied to the raw EMG signal, with a subsequent digitally-applied band-pass filter between 10 and 500Hz. All collected signals were then rectified and smoothed using a root mean square calculation with a 100ms window, as used elsewhere.[235]

5.2.4.6 Median frequency (MF)

MF was measured post-processing from the sEMG muscle signal and was calculated by the point at which the area of the power spectral density was divided in half.[235] The analysis of MF from EMG muscle signals results in an estimation of the electrical conduction properties of the tissues

underlying the surface electrodes and is thereby associated with muscle fiber conduction velocity changes.[235, 236] More specifically, during sustained isometric contractions (ie. Sorensen test) there is an approximate linear relation between conduction velocity and power spectral frequencies.[236] Therefore, muscular fatigue can be examined from the relationship between average muscle fiber conduction velocity and frequencies of the EMG power spectrum.[236] In the current study, the rate of decline in MF was measured as changes to the EMG frequency spectrum using a fast Fourier transformation algorithm, and assessed at relative time points of each participants' total Sorensen duration time (5% epochs of normalized time points representing each 20% of duration time). Average median frequency (L4/L5) per epoch was calculated using the average of right and left lumbar erector spinae muscles, with MF slope plotted relative to time (0 to 100) of Sorensen total duration.

5.2.4.7 Kinematics (spinal displacement)

Spinal kinematics were assessed using a dual-sensor three-dimensional (3D) motion analysis electromagnetic tracking system (Patriot, Polhemus Inc., USA). The Patriot system (6df, 60Hz/sensor, <18.5ms latency) involved the use of a transmitter as a reference point for two sensor receivers by emitting a magnetic field detected by the two receivers. It allowed for the collection of biomechanical data on position and orientation, by simultaneously computing the real-time movement of the two sensors through space. Motion tracking included movement in the X (sagittal plane), Y (transverse plane) and Z (coronal/frontal plane) rotational axes. The two electromagnetic motion trackers were placed on the surface of the skin overlying the T12 and S1 vertebrae. Data collected was digitally processed through the PiMgr for Microsoft Windows computer software. Spinal sagittal movement was defined as the total spinal displacement in the sagittal plane (X axis, anteroposterior direction) relative to the transmitter reference point (sampled prior to Sorensen test commencement).

5.2.5 Statistical analysis

Statistical analysis was performed using SPSS v23 (IBM, USA). Normality testing of all collected variables was assessed using a number of methods, including Kolmogorov-Smirnov and Shapiro-Wilk tests, in addition to the examination of frequency histograms and values of skewness and kurtosis. Results of normality testing indicated some variables were not normally distributed, so a combination of parametric and non-parametric methods were used. Correlation analysis was performed to examine relationships between Sorensen duration, sagittal movement, MF slope, pain and measures of anthropometrics and adiposity. Pearson correlation coefficient was used for parametric variables and Spearman's correlation was used for non-parametric variables. Variables that were significantly correlated to Sorensen duration were used as the predictor variables for mediation and regression analysis. Collinearity was assessed from the correlation analysis, whereby highly correlated variables ($r>0.90$) were considered collinear and therefore excluded from further analysis. Variables that were not found to be correlated with primary predictor variables were not included in the mediation analysis.

Mediation was performed with bootstrapping techniques using the custom written macro PROCESS (www.processmacro.org), which was downloaded into SPSS. Mediation analysis investigates the effect of a causal variable X on a proposed outcome Y through one or more mediating variables M.[237] Simple mediation involves a single intervening variable, whereas multiple mediation analysis occurs in the context of simultaneous involvement from multiple variables.[237] Bootstrapping involves drawing repeated samples (minimum 1000) with replacement from the original sample to approximate the sampling distribution of the indirect effect.[237, 238] Since this method is based on estimation rather than the assumption of normality,[237] it is considered more powerful than traditional methods such as Baron and Kenny's[239] causal steps approach, the Sobel test and empirical M-test

which require more assumptions than bootstrapping.[238] For example, the Sobel test assumes normality of the sampling distribution of indirect effects, which tend to be asymmetrical.[238] Alternatively, the bootstrap method can be used to make inferences about indirect effects in the majority of models,[237, 238] with reduced risk of estimation inaccuracy and type I error.[238] Furthermore, bias-corrected bootstrapping has been recommended in multiple mediation contexts,[237] which is a known limitation of the causal steps approach.[240]

The following a priori conditions had to be successfully met to confirm mediation: 1) X variable (independent variable) was significantly associated with Y variable (dependent variable) (total effect; *c* path, Figure 5.3); 2) X variable was significantly associated with one or more proposed mediator variables (M) (*a* paths, Figure 5.4); 3) each of the proposed mediators was significantly associated with Y (b paths); and 4) the relationship between X and Y variable was reduced (direct effect, *c'* path) when controlling for the proposed mediators (indirect effect, *a* x *b*), with the 95% confidence interval for the indirect effect of each proposed mediating variable outside 0.

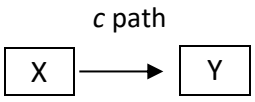

Figure 5.3 Total effect of X variable on Y variable (c path)

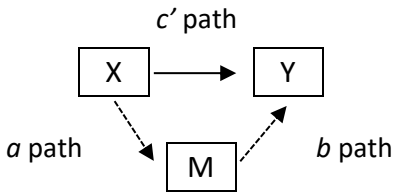

Figure 5.4 Direct (c' path) and indirect effects (a x b path) of X variable on Y variable when controlling for M variable

Four mediation models were performed (PROCESS, model 4) to examine whether the proposed mediators (pain change, sagittal movement) influenced the relationship between anthropometric and adiposity variables (weight, BMI, WC, TC-TBF) with Sorensen duration. Statistical significance was set at $p<0.05$.

5.3 Results

Correlation analyses showed that Sorensen duration was associated with weight, BMI, WC, WHR and TC-TBF (Table 5.2). No significant associations were observed between Sorensen duration and A-L, MF slope or sagittal movement. MF slope was not related to the Sorensen or any anthropometric or adiposity variables. A-L was found to be correlated with End pain (r=0.388, p=0.004) and Pain change (r=0.342, p=0.013).

Mediation models were performed for weight, BMI, WC and TC-TBF, with respect to Sorensen time. No mediation analysis was performed for WHR since not all required criteria were met. The total effect (*c* path) of all four models was statistically significant: weight (B=-1.570, r=0.371, p<0.001), BMI (B=-4.319, r=0.307, p<0.001), WC (B=-1.785, r=0.319, p<0.001) and TC-TBF (B=-34.040, r=0.159, p=0.005). Weight, BMI, WC and TC-TBF were significantly associated with end pain and pain change, but end pain was excluded due to high collinearity (r=0.836, p<0.001). TC-TBF was also associated with sagittal movement (Table 5.2). Neither of the proposed mediators (pain change, sagittal movement) were significantly associated with Sorensen time. Since only two of the four required steps to confirm mediation were met, no further analysis was performed.

Table 5.2 Correlations between task performance (Sorensen) with anthropometric, spinal movement, pain and muscle endurance outcomes

	1	2	3	4	5	6	7	8	9	10
1. Sorensen	-									
2. Weight	-.542†**	-								
3. BMI	-.453†**	.818†**	-							
4. WC	-.478†**	.847†**	.876†**	-						
5. WHR	-.519^**	.558†**	.470†**	.704†**	-					
6. TC-TBF	-.370^**	.211†	.171†	.251†	.063^	-				
7. Sagittal	.197†	-.163†	.019†	-.101†	-.144†	-.334†*	-			
8. End Px	.181^	-.361†**	-.320†*	-.335†*	-.148^	-.434^**	.035†	-		
9. Px Change	.269^	-.424†**	-.359†**	-.419†**	-.225^	-.415^**	.167†	.836^**	-	
10. MF slope	-.148^	-.074†	-.202†	-.071†	-.015^	.120^	-.059†	-.164^	-.169^	-

BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio; TC-TBF, total circumference relative to total body adiposity ratio; Sagittal, spinal movement in the sagittal plane; End Px, self-reported pain at test cessation; Px Change, change in self-reported pain from start to test cessation; MF slope, rate of decline in median frequency as indicator of lumbar muscle endurance

† Spearman's rho

^Pearson Correlation

*****Correlation significant at p<0.01 level***

****Correlation significant at p<0.05 level***

5.4 Discussion

The main findings of this study showed that Sorensen duration was associated with weight, BMI, WC, WHR and TC-TBF, but not A-L, MF slope or sagittal movement. Based on these findings, the hypothesis that increased body mass and its distribution would be related to poorer Sorensen task performance was supported. Similar to previous research,[211] significant correlations were identified between A-L and self-reported pain, but particularly the pain experienced at test cessation. Changes in task-induced pain were also found to be moderately correlated with weight, BMI, WC and TC-TBF. Results of the mediation analysis indicated strong relationships between Sorensen duration and predictor variables (weight, BMI, WC, TC-TBF), but mediator variables (pain change, sagittal movement) had minimal influence on the models. Therefore, the relationship identified between body mass distribution and Sorensen duration was not explained by increased spinal flexion or faster rates of muscle fatigue as hypothesised.

The link between A-L and end pain but not task duration, may suggest that increasing abdominal adipose tissue is associated with greater task-induced pain development. In addition, the moderate correlations observed between pain change and measurements of body mass, body composition and adiposity distribution may indicate that pain is a common denominator among such measurements in cLBP populations. Since body mass measures contributed to Sorensen duration but A-L did not (despite associations with pain), it may indicate that the restricted nature of the task to a specific position prevented the manifestation of an A-L effect. For instance, within the context of the testing procedure, individuals were required to maintain an isometric horizontal position with the upper body unsupported and arms folded across the chest. Each participant was prompted when necessary to correct their posture, such as by lifting their head and shoulders back up to the starting position. If they weren't able to amend their position within five consecutive seconds the test was terminated.

By restricting the within-test variation in this manner, it may have reduced the capacity of the test to exhibit an effect of A-L disparity on test duration. For example, limiting the degree of upper body movement, possibly altered the natural posture that individuals may have otherwise adopted. The test was controlled to this extent to ensure validity and comparability of the results, but in doing so may have also concealed differences in A-L effects on posture throughout the task.

Moreover, TC-TBF was found to be related to Sorensen duration, although the relationship was weaker than more simplistic body mass measures. Since TC-TBF refers to subcutaneous adiposity of the mid-section proportional to total body adiposity, it may indicate relative adiposity distribution in a similar but less specific manner to the A-L. Of all predictor variables measured, sagittal movement was only found to be correlated with TC-TBF. This may be due to its specificity as an adiposity measurement, whereby increased central adipose tissue places greater demand on the spine and leads to acute spinal flexion and faster muscle fatigue. Conversely, sagittal movement was not related to WHR, despite the significant correlation between WHR and Sorensen duration. Therefore, perhaps there is a common element underpinning a relationship between spinal movement and trunk adiposity distribution, but not overall trunk mass. Another possibility may be that in individuals with higher A-Ls, they are in a prolonged state of increased lumbar flexion or spinal hyperlordosis from the excess anterior adipose tissue. The concurrent risks accompanying such a state have been well-documented in the past. For example, a flexed posture has been shown to reduce the capacity of the spine to tolerate shear forces,[164] and the yield point of spinal compressive loading is reduced with a flexed failure posture.[165] As a result, it has been stated that the amalgamation of both prior loading history and a flexion-based posture alters the compressive strength and mode of failure of the spine.[165] If a chronic state of increased spinal lordosis was present in cLBP sufferers with higher anterior to posterior loading ratios, it may infer a pre-task discrepancy of spinal positioning between those with higher compared to lower A-Ls. Since the degree of spinal flexion was not measured prior to the test (separate to the reference position), it is difficult to confirm or refute this possibility.

However, it may support the need for further research in this area, particularly if an A-L effect may have been observed if the task was not controlled so diligently.

The identified relationships between mass measurements (weight, BMI, WC) and Sorensen time were of moderate strength and negative direction, indicating that less favourable body composition or body mass resulted in poorer task performance. It is plausible for this result to be attributed to the degree of loading of the test. For example, previous research has shown that the Sorensen test performed at 100% of the head-arms-trunk (HAT) segment is not a sufficient load to reveal differences between people with and without LBP symptoms.[226] Furthermore, this has been observed despite decreasing endurance times for increasing HAT segment loading.[226] Although 100% HAT loading has previously showed no differences between people with LBP and those without, segmental loading at 160% HAT was found to reduce task duration by 40% among those with LBP.[226] The population tested was not cLBP-specific, but such findings may still be of relevance. For example, it is possible that the 100% HAT loading used for the Sorensen test in the current study was not adequate to reveal a true pain mediation. Moreover, this segmental loading consideration may also play a role in the apparent lack of effect of A-L on Sorensen duration. It may be reasonable to believe that had the HAT loading been increased above 100%, negative consequences of larger A-Ls on task performance may have been observed.

Although this study's findings have demonstrated that mass may impact task performance in people with cLBP, it remains unknown why they perform more poorly in the Sorensen test. Since both spinal flexion and rate of MF decline were not related to or predictors of test duration, the results of the current study did not fully explain Sorensen performance. In addition to HAT loading considerations, it is possible that the test itself may have produced an inadequate representation of muscle fatigue. For example, it has previously been argued that increases in hip extensor activity and other

alternative strategies of load-sharing may prolong test duration, and therefore provide an inaccurate reflection of lumbar muscle endurance.[226] Moreover, LBP sufferers may exhibit higher resistance to fatigue, by employing altered physiologically-coordinated muscle strategies to compensate for a lower level of lumbar muscle endurance.[226] An alternative suggestion is that pain augmentation may be an indirect result of increased body mass parameters, or the consequence of adiposity distribution. Assuming this was the case, perhaps such effects were simply not revealed in the context of the postural task tested. It was reasonable to believe that greater abdominal adiposity may provoke flexion-induced LBP symptoms and muscle fatigue in a postural task, but it was not confirmed in the current study. However, it does not necessarily conclude that such an effect would also fail to be seen in different experimental contexts.

Although no earlier studies have explored the effect of relative adiposity distribution on the Sorensen test, body mass indices have been included in the past. Such measurements have consisted of body weight,[241, 242] %TBF,[243] BMI and the Davenport index,[234, 244] yet these studies have produced inconclusive results. For example, two studies have used BMI and the Davenport index, one involving adult men and women with cLBP[244] and the other healthy men and women.[234] In the cLBP study, there were no differences identified in muscle endurance between obese and non-obese individuals.[244] Irrespective of the disparity in outcome measures used, the results of the current study indicated a similar finding of no relationship between A-L and lumbar muscle endurance in cLBP. Alternatively, researchers in the second study on healthy men and women observed an inverse relationship between BMI and paraspinal muscle fatigue, which was more apparent at the L4/L5 than L1/L2 level.[234] Moreover, differences have also been found among earlier studies involving body weight.[241, 242] For instance, one study identified reductions in static lumbar endurance time with increasing weight,[241] yet another found no significant correlation between body weight and endurance[242] despite assessing comparable population samples. Furthermore, %TBF has also been shown to contribute to static lumbar muscle endurance time,[243] although the presence or absence of pain in

the study population was not classified. Such inconsistency among research studies makes it difficult to draw conclusions regarding the effect of body mass parameters on the Sorensen test. However, these previous findings may support the notion of increased anterior force on the lumbar spine coinciding with larger A-Ls, and potentially greater lumbar muscle fatigue to compensate these forces. It is possible that the discrepancy among research may be explained by the inclusion of pain change in the mediation models of the present study. For example, perhaps there is an underlying mechanism of pain interference with the observation of an abdominal loading-fatigue interaction, which is otherwise shown in healthy populations. For this reason, it may be necessary to further compare healthy and cLBP populations performing the Sorensen test, to better understand potential influences of adiposity and body mass measures on muscle endurance and task duration. Furthermore, the potential influence of psychological factors on task performance cannot be ruled out. In a previous Sorensen study, negative beliefs about back pain and greater psychological disturbance (combined somatic symptoms and self-rated depression) were predictors of underperformance among those with cLBP. It was observed that 22% of the variance in expected versus actual task duration was explained by such psychological factors.[229]

The novel aspect of this study lends itself to potential constraints. For example, the findings may reflect the possibility that the current nature of the Sorensen task did not permit an A-L effect to be fully manifest. Moreover, there is existing debate within the literature regarding the validity and relevance of the MF method for the assessment of muscular fatigue.[223, 245] This may suggest that MF was not the most appropriate method to use for the present study, regardless of its common use in Sorensen test research.[223, 226, 231, 234, 245] Therefore, the finding that MF slope was not related to Sorensen duration or anthropometric and adiposity measurements may suggest that body mass has no impact on lumbar muscle fatigue. However, it cannot be concluded that this result would be replicated with the use of an alternative fatigue method. Regardless of such methodological

considerations, study findings imply that upper or total body mass and its relationship to pain may play a role in the Sorensen test.

5.5 Conclusion

Further research is needed to support or refute the findings of the present study and continue to investigate the complex relationship between obesity and cLBP. More specifically, future studies should look to explore anthropometric and adiposity variables in other postural tasks, and perhaps in comparison between cLBP and healthy populations. The results of this study have added to previous research findings, through the confirmation of a relationship between body composition and distribution with self-reported pain in cLBP sufferers. The evidence suggests that there may be an interaction between spinal positioning, mass distribution and pain that should continue to be explored in the future.

Chapter 6: General Discussion and Conclusion

6.1 Summary and Interpretation of Main Research Findings

The aim of this thesis was to investigate the relationship between obesity and cLBP, and explore possible factors mediating that relationship. The primary research findings support the hypothesized association between abdominal adiposity and pain, but not disability, among people with cLBP. Although body mass distribution negatively affected task performance in cLBP individuals, abdominal adiposity was not related to performance for the task employed. The hypothesis that spinal movement and lumbar muscle fatigue would mediate obesity and cLBP during postural performance was not supported.

Past research has provided evidence of a relationship between obesity and cLBP,[23, 71-80] with common findings linking BMI and cLBP,[23, 73, 74, 78, 81] or general LBP.[68, 77, 142] Although there was heavy reliance on BMI in previous LBP research,[71, 74, 76, 78, 139] limitations of the measure were raised.[73, 80] Such research also highlighted several inconsistencies, including poor BMI classification regarding cutoff points and unclear delineation between overweight and obesity categories.[97] Earlier conclusions indicated a lack of definitive evidence to link BMI-based obesity with LBP.[77] The results of Study 1 of this thesis provide clarification and understanding of earlier research findings. For example, since no relationships with BMI and pain or disability (including changes) were observed, it is evident that BMI should not be relied on as the sole outcome measure of obesity in cLBP research. Alternatively, it has been proposed that adiposopathy needs to occur in combination with an elevated BMI for musculoskeletal pain to be experienced.[152] For instance, adipocyte immune cells in an adiposopathic state may act similarly to bacterial infection or autoimmune disease.[152] However, adiposity may not

always result in chronic inflammation.[152] This notion may explain the lack of consistent correlation between increased BMI and LBP symptoms, particularly if chronic systemic inflammation induced by changes to adipocyte metabolic activity only takes place in certain individuals.[152]

The findings of Study 2 support the need for greater consideration of adipose tissue and its distribution in the obesity-cLBP relationship, rather than focusing on simplistic anthropometrics. Adipose tissue distribution has been implicated in the past, since it was found to be more closely related to risk of cLBP than BMI.[112] Although not of a chronic nature, associations between obesity and LBP have been shown in the upper percentages of BMI only,[142] presumably indicating greater adiposity since adipocyte size increases with rising BMI.[152] It is known that cLBP prevalence escalates with increasing WC, WHR and BMI,[73] and the results of Study 2 showed that self-reported pain was associated with adiposity distribution. Such findings may help explain the stronger BMI-LBP associations with higher BMI percentages observed in the past. Moreover, Study 2 showed that relative abdominal-to-lumbar adiposity (A-L, A-L/WHR, A-L/BMI) was associated with cLBP, which may support the integral role of adipose tissue in obesity-cLBP pathophysiology. Recent research has also reported relationships between adiposity and pain.[149-151] For example, fat mass and the fat mass index (FMI; DXA-derived fat mass / height^2) as well as traditional body weight and BMI, have been significantly associated with increased risk of multisite pain, pain at weight-bearing body sites, hand pain and pain at a greater number of lower body sites.[149, 151]

Although the novel findings of Study 2 indicated that abdominal adiposity distribution relative to trunk or total body size is important in the obesity-cLBP relationship, explanations for such associations were still unclear. Early research into obesity and LBP had concluded it was unknown if the relationship was causal.[14, 75, 77] Other studies proposed the obesity-pain relationship may be mediated by multiple interrelated factors.[67, 70] The possibility of a bi-directional link between obesity

and pain was also suggested,[116] or that obesity may be a marker for a true causal factor.[72] For this reason, Study 3 was an exploration of such possibilities, within the context of a gravity-counteracting postural task of the Sorensen test. The findings indicated that body mass and its distribution were linked to poor Sorensen performance, and supported the correlation between A-L and cLBP observed in Study 2. In Study 3, weight, BMI, WC and TC-TBF were also associated with pain change throughout the test, although mediation of such variables was not confirmed. Moreover, the relationship between body mass distribution and test performance was not explained by spinal movement or lumbar muscle fatigue. Therefore, it is possible that there may be two different mechanisms of action involved. For example, perhaps the A-L correlation to cLBP may indicate a metabolic mediation, whereas the anthropometric variables may suggest more of a mechanical role. Such suggestions have also been recently raised in research on body composition and multisite pain. Two separate studies proposed metabolic factors were implicated in multisite pain pathogenesis.[149, 151] Fat mass or body weight was said to play an important part, with a systemic role likely due to the association between fat mass and hand pain, which is not a weight-bearing site.[151] This was supported by the second study, in which the same association to pain at lower body sites was not observed for fat-free mass.[149] However, a possible biomechanical loading effect was also suggested, since fat mass, FMI and BMI were linked to pain at all weight-bearing sites.[151] Consequently, it may be possible for the findings of Study 3 to be corroborated should similar research be conducted in the future. Although mediation possibilities including contributions of spinal movement and adiposity distribution to mechanical loading in the obesity-cLBP relationship were not identified, they may still be of relevance. Furthermore, this finding does not rule out the possibility of observing an A-L effect in a different postural task or testing situation. In either instance, Study 3 confirmed a connection between body composition and cLBP.

The importance of abdominal adiposity and body mass distribution on cLBP identified in this thesis has been supported by the possibility that obesity-induced mechanical loading of the lower back region may be dependent on body morphology, or somatotype.[147] For example, a recent study on body segment inertial parameters observed increases in both trunk moments of inertia and radii of gyration.[147] It was suggested that central adiposity is likely to have negative implications for spinal loading, on the basis of increased trunk moments of inertia and injury risk through near-maximal torque estimates.[147] The authors further raised the probability of earlier onset of neuromuscular fatigue in repetitive tasks, and substantial cumulative impacts during walking and carrying over the long-term.[147] Therefore, it is reasonable to believe that back pain may be the net result, particularly when occurring for prolonged periods of time. For example, this may be the case for central adiposity-obese individuals, or those with an increased A-L. Abdominal adiposity accumulation may also result in greater daily mechanical loading of the lumbar spine through compressive and shear forces, since increased abdominal and sagittal diameters have been associated with greater odds of severe lumbar disc degeneration.[148]

Evidently, there is still controversy among obesity-LBP research. For example, authors of a recent study on various anthropometric measures and LBP, suggested central adiposity doesn't explain LBP occurrence.[246] This was due to the finding that all body size measures (body weight, BMI, WC, WHR, hip circumference) were significantly related to LBP risk in both genders, after age adjustment.[246] They also found that significant associations between WHR and LBP were greatly reduced after adjustment for other risk factors.[246] Since the results of this thesis suggest A-L relative to WHR or BMI were the strongest predictors of cLBP, the adiposity to size ratio may be paramount. Alternatively, perhaps the primary issue is the sole usage of fat mass measurements or simplistic body size measurements, such as WHR, BMI or WC. Fat mass to muscle mass ratio may also warrant consideration, since high fat mass-to-muscle ratios have been recently linked to increased

musculoskeletal pain.[247] As a result, research on obesity and cLBP may require a more holistic and comprehensive consideration of body composition, relative to body size and shape. The importance of body composition may allude to a series of interrelated factors that lead to the pain expression underpinning several musculoskeletal pain pathologies. Perhaps it is not the separation of mechanical or inflammatory mediation possibilities that is most important, but rather the consideration of potentially intertwined variables that is of significance. For example, adiposity-induced chronic low-grade inflammation is a known contributor to atherosclerosis, which has been linked to disc degeneration.[148] Such deliberations also originate from the assumption that all cases of cLBP or LBP are pathologically identical, which is unlikely given the physiological complexity of the human body and vast opportunity for biological variation. Therefore, there may not be one simple explanation, cause or mediation that encapsulates the overall obesity-cLBP relationship.

6.2 Limitations of the Research

The conflicting nature of previous research into obesity and cLBP or related parameters (LBP, BMI, body weight) lends itself to careful consideration of study limitations. One potential constraint is the exercise program in Study 1 was based on cLBP treatment and not BMI modification. A program tailored towards body mass manipulation with monitoring of inflammatory blood markers may have shed more light on the results, providing a firmer conclusion of evidence and increased understanding of previous findings. Such mass manipulation and inflammation studies relating to Study 2 may have also been beneficial. However, previous research had relied on the BMI measurement, provided inconclusive evidence between obesity and LBP, and lacked thorough exploration of adiposity and pain linkages. Therefore, it was believed to be more important to first examine BMI in the context of common exercise-based cLBP treatment, and establish baseline relationships between adiposity and cLBP.

Another limitation of Study 2 was the subjective nature of US methodologies. Since each image must be individually measured by the researcher, bias or intra-rater error is a possibility. Potential bias may have been reduced by including a comparison to CT or DXA, but such methods are expensive and would have rendered US unnecessary. Moreover, US is an established valid and reliable method of assessing abdominal adiposity compared to gold standard methods.[32, 90, 182-184, 186] Lastly, only one postural task was employed in Study 3, with no specific gender or non-cLBP comparison included. As neither gender or non-cLBP populations were the focus of this thesis, it was a constraint considered to be outweighed by the primary aim of the research.

6.3 Thesis Research Output

Two scientific journal articles[197, 211] have been produced as a result of the research conducted in this thesis, and have been published in internationally known peer-reviewed journals. *Spine* has an impact factor of 2.439 (Journal Citation Reports, JCR; 2015) and a 5-year impact factor of 2.786 (JCR, 2015). *BMC Public Health* is an open-access journal with an impact factor of 2.209 (JCR, 2015) and a 5-year impact factor of 2.746 (JCR, 2015). The two published journal articles[197, 211] resulting from this thesis have been cited 8 times, as at 9 May 2017. Therefore, the work of this thesis is of publication quality with important contributions to research and clinical contexts.

6.4 Research and Clinical Implications

The value of this work is two-fold, as it contributes to both obesity and cLBP research fields. Despite the precise etiology and interaction remaining unknown for obesity and cLBP as well as other related conditions, it is clear that they are no longer separate entities. As described earlier in this thesis, the majority of previous research focused on general LBP using BMI as a single obesity measurement. Consequently, some studies may need to be repeated in the context of cLBP populations, with the inclusion of multiple obesity measures to assess body size and composition. It is evident that a large scope of research remains to be explored regarding linkages between obesity and cLBP. For example, consideration of a possible inflammatory pathway within the obesity-cLBP relationship may be examined through exercise or nutrition-based intervention studies, with a focus on manipulation of body mass or body composition. Other research possibilities may include neuromuscular consideration in integrated obesity-cLBP studies, thresholds of central adiposity and their effect on pain, the biomechanics of an obese state, adiposopathy and metaflammation interactions with pain manifestation, and potential linkages to other musculoskeletal pain conditions. Regardless of the vast research potential remaining in this area, the work of this thesis is innovative and novel. Relationships between BMI and exercise-induced cLBP changes had not been previously explored, and past studies had lacked consideration for possible associations between adiposity distribution and cLBP. Moreover, the notion of mass distribution and mechanistic mediation during a postural task in the obesity-cLBP relationship had not been previously examined.

The research resulting from this thesis also has clinical implications through evidence-based treatment recommendations for practitioners. For example, it is reasonable to believe that the treatment approach of obese individuals and cLBP sufferers should be reflective of the established association between the two conditions. Such considerations may include exercise prescription

tailored towards the reduction of abdominal adipose tissue, or the attainment of a more favourable body composition. These possibilities may not necessarily instigate direct changes to obesity or cLBP treatments, but rather promote a more holistic approach to the prescribed treatment. Instead of practitioners treating obesity and cLBP as separate health problems, they may consider them as an interrelated condition of sub-optimal wellbeing. In doing so, the work of this thesis may help to improve clinical treatment efficacy.

6.5 Overall Concluding Remarks

This thesis has indicated that obesity and cLBP are related conditions. Study 1 showed that BMI may not be the most appropriate obesity measure to use for cLBP research, particularly in isolation. Study 2 and Study 3 have indicated that adiposity and its distribution around the body is important for cLBP, particularly when considered relative to overall body size and shape. Although no mediation between A-L, lumbar muscle endurance or sagittal spinal movement with Sorensen task performance was identified for the obesity-cLBP relationship, it does not rule out the possibility of effects being observed in alternative research contexts. It is evident from the work of this thesis that consideration of adipose tissue and its distribution may be paramount in chronic pain pathologies. A large scope of research still remains to be explored, but this research has contributed to the body of evidence linking obesity with cLBP. This thesis has demonstrated the importance of the work within the obesity and cLBP fields. Two journal publications have been produced and there is clearly a growing interest in this research area among the scientific community. The work of this thesis provides a strong foundation to an extremely relevant issue.

Chapter 7: References

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