Chronic obstructive pulmonary disease and cervico-thoracic musculoskeletal dysfunction

by

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Abstract

Conservative non-pharmacological evidence-based management options for Chronic Obstructive Pulmonary Disease (COPD) primarily focus on developing physiological capacity. With co-morbidities, including those of the musculoskeletal system, contributing to the overall severity of the disease, further research was needed. This thesis presents a critical review of the active and passive musculoskeletal management approaches currently used in COPD. The evidence for using musculoskeletal interventions in COPD management was inconclusive. Whilst an evaluation of musculoskeletal changes and their influence on pulmonary function was required, it was apparent that this would necessitate a significant programme of research. In view of this a narrative review of musculoskeletal changes in the cervico-thoracic region was undertaken. With a paucity of literature exploring chest wall flexibility and recent clinical guidelines advocating research into thoracic mobility exercises in COPD, a focus on thoracic spine motion analysis literature was taken. On critically reviewing the range of current *in vivo* measurement techniques it was evident that soft tissue artefact was a potential source of measurement error. As part of this thesis, soft tissue artefact during thoracic spine axial rotation was quantified. Given the level was deemed unacceptable, an alternative approach was developed and tested for intra-rater reliability. This technique, in conjunction with a range of other measures, was subsequently used to evaluate cervico-thoracic musculoskeletal changes and their relationship with pulmonary function in COPD. In summary, subjects with COPD were found to have reduced spinal motion, altered posture and increased muscle sensitivity compared to controls. Reduced spinal motion and altered neck posture were associated with reduced pulmonary function and having diagnosed COPD. Results from this thesis provide evidence to support inception of a clinical trial of flexibility or mobility exercises in COPD.

Dedication

I lovingly dedicate this thesis to my husband John, children Rosy and Michael and lifelong friend Annabel. Without their unfaltering support this research would not have been possible.

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I would like to thank wholeheartedly Dr George Balanos, my first supervisor, who offered me the chance to fulfil a long-held wish to explore this field of research and to undertake a doctorate. I am also extremely grateful to Dr Peymane Adab, who came on board as my second supervisor part way through the doctorate, providing a great deal of support in completing the final study.

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AAOMPT	American Academy of Orthopaedic Manual Physical Therapists
AMED	Allied and Complimentary Medicine Database
APTA	American Physical Therapy Association
ATS	American Thoracic Society
BMD	Bone mineral density
BMI	Body mass index
CENTRAL	Cochrane Central Register of Controlled Trials
CINAHL	Cumulative Index to Nursing and Allied Health Literature
COAD	Chronic obstructive airflow disease
COLD	Chronic obstructive lung disease
COPD	Chronic Obstructive Pulmonary Disease
CRD	Centre for Research and Dissemination
DARE	Database of Abstracts of Reviews of Effects
DXA	Dual-emission X-ray absorptiometry
EMBASE	A biomedical and pharmacological database
EMG	Electromyography
ERS	European Respiratory Society
ERV	Expiratory reserve volume
FEF	Forced expiratory function
FEFR	Forced expiratory flow
FEV_1	Forced expiratory volume in one second
FVC	Forced vital capacity
$FEV_{1/}FVC$	Ratio of forced expiratory volume in one second and forced vital capacity
FRC	Functional residual capacity
GOLD	Global Initiative for Chronic Obstructive Lung Disease
HADS	Hospital Anxiety and Depression Score
HVLAT	High velocity low amplitude thrust

IFOMPT	International Federation of Orthopaedic Manipulative Physical Therapists
IC	Inspiratory capacity
ICC	intra-class coefficients correlation
ICL	Index to Chiropractic Literature
MCID	minimum clinically important difference
MEDLINE	Medical Literature Analysis and Retrieval System Online
MET	Muscle energy technique
MRC	Medical Research Council
MRT	Myofascial release technique
MVV	Maximum voluntary ventilation
NDI	Neck Disability Index
NICE	National Institute for Clinical Excellence
NRS-N	Numerical rating scale-neck
NRS-B	Numerical rating scale-back
O_2sat	Oxygen saturation
ODI	Oswestry Disability Index
OMT	Osteopathic manipulative therapy
OR	Odds ratio
PO2	Partial pressure of oxygen
PCO2	Partial pressure of carbon dioxide
PNF	Proprioceptive neuromuscular facilitation
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses Guidelines
QOL	Quality of life
RCT	Randomised control trials
RMSG	Respiratory muscle stretch gymnastics
RV	Residual volume
SCM	Sternocleidomastoid
SD	Standard deviation

SEM	Standard error of the means
SGRQ	St George's Respiratory Questionnaire
STA	Soft tissue artefact
STM	Soft tissue massage
STROBE	Strengthening the Reporting of Observational studies in Epidemiology
SVC	Slow vital capacity
TLC	Total lung capacity
TGV	Thoracic Gas Volume
TLP	Thoracic lymph pump
TPI	Trager Psychophysical Integration,
URTI	Upper respiratory tract infection
VC	Vital capacity
VAS	Visual analogue scale
WHO	World Health Organisation

Chapter 1. INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is 'a common, preventable and treatable disease, characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and lungs to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients' (GOLD, 2011).

COPD, as a chronic progressive disease leads to considerable loss of quality of life and early mortality. It is expected to become the fourth leading cause of death by 2020 (Patel & Hurst, 2011) and the third by 2030 (GOLD, 2011). In the UK around 3 million people have COPD, although ~2 million of these are undiagnosed (Healthcare Commission, 2006). Prevalence of diagnosed COPD is estimated to be around 1.6% in England, equivalent to 819,524 people (NICE, 2010).

The most recent data reported that, in the UK, COPD costs the NHS an estimated £800 million per year in direct healthcare costs or £1.3 million per 100,000 people (Department of Health, 2005). Furthermore, an estimated 24 million working days were lost per year in the late 1990's due to COPD, with a resultant £2.7 billion in lost productivity (Department of Health, 2005). The high social and financial costs associated with managing this disease are set to rise further given longer life expectancy and evidence that currently many cases go undiagnosed (Wise, 2006; Fromer, 2011).

1.1. COPD: an overview of the disease

The development of COPD is multifactorial with genetic and environmental factors influencing risk (GOLD, 2011; Vijayan, 2013). A complex disease, its effects extend beyond airflow obstruction and it is characterised by a number of anatomical, pathophysiological and clinical

features. Whilst long considered a disease of the lungs, in recent years the impact on other body systems has been extensively reported, with these co-morbidities often contributing to poorer levels of functional capacity, dyspnoea, health-related quality of life and increased mortality (Cooper & Dransfield, 2008; Barnes & Celli, 2009; GOLD, 2011). Whilst it goes beyond the scope of this thesis to consider these in detail, the following section provides an overview of the anatomical, pathophysiological and clinical features of COPD, principally relating to the lung and musculoskeletal system.

1.1.1. Anatomical

Anatomical features of COPD include both intra and extrapulmonary structures. Intrapulmonary anatomical changes are likened to those of older age non-smokers (Jarad, 2011), affecting the small airways, such as bronchioles. Structural abnormalities are a consequence of pathophysiological changes (described in detail in section 1.1.2) and include peribronchiolar fibrosis, mucus plugging and the loss of alveolar attachments due to air trapping. These changes result in destabilisation of the airways related to reduced elastic recoil.

The most widely reported and researched extrapulmonary feature includes changes to skeletal muscle and bone structure and function. Several postural changes are classically attributed to COPD and recognised as clinical signs of disease in physiotherapy textbooks. These include barrel shaped chest, forward head posture, and protracted shoulder girdles, (Chaitow, 2002). Despite this, there are no studies that have specifically investigated postural changes in COPD. 'Upper crossed syndrome' is a term coined by an osteopath called Garland (Chaitow, 2002) to broadly describe a forward head posture and protracted shoulders which results from a tendency to breathe using the upper-chest muscles. Such changes are often associated with dyspnoea and hyperinflation, with the latter being a consequence of airway narrowing due to inflammation and air trapping. Hyperinflation is diagnosed most commonly using x-ray, where flattening or depression of the diaphragm can be seen along with an increase in the retrosternal

airspace and a more horizontal orientation of the ribs. Clinically, hyperinflation is associated with increased activity of accessory respiratory muscles with subjects tending to lean forward and fix the pectoral girdle with their arms to assist rib cage expansion (Chaitow, 2002). Whilst it would appear reasonable to presume that these changes are progressive with increased disease severity, there has not yet been a systematic evaluation of such in a COPD cohort.

This thesis explores and reports on changes in the thoracic cage with respect to bone and joints and cervico-thoracic skeletal muscles. It is however beyond the scope to critically discuss structure and function of the diaphragm, the principle inspiratory muscle, and peripheral skeletal muscles, which are comprehensively reviewed elsewhere (Man *et al.*, 2009; Donaldson *et al.,* 2012).

1.1.2. Pathophysiology

Expiratory flow limitation is the pathophysiological hallmark of COPD and a consequence of chronic airway limitation (O'Donnell & Parker, 2006). Exacerbations, usually resulting from exposure to noxious particles such as tobacco smoke, pollutants or bacteria, reflect worsening of the disease and lead to further expiratory flow limitation. The pathological changes in central airways, small airways and alveoli arise from complex immunological mechanisms resulting in systemic inflammation, apoptosis and ineffective repair leading to structural changes in the airways (GOLD, 2011; Vijayan, 2013). It is hypothesised that some extrapulmonary features and co-morbidities of COPD are a consequence of systemic inflammation, purported a spillover from processes originating in the pulmonary tissue (Patel & Hurst, 2011). Pro-inflammatory markers, such as metalloproteinase-9 have been linked to enhanced bone re-absorption in COPD (Kochetkova *et al.,* 2012). The proposed mechanism for this observation is through degradation in type I collagen. It is also possible for this process to affect other musculoskeletal structures of the thoracic cage, such as hyaline costal cartilages or ligaments, which could in turn, adversely affect the biomechanics of respiration. From published reviews detailing the pathophysiology of

COPD (O'Donnell & Parker; 2006; Barnes & Celli, 2009) it is notable that little consideration has been given to this as yet.

1.1.3. Clinical features

As well as chronic cough, dyspnoea, pursed lip breathing and chronic sputum production, other clinical features of COPD may include fatigue, cachexia, and anorexia (GOLD, 2011). Such symptoms are important prognostically and potentially indicative of co-morbidities such as cancer, pulmonary hypertension, ischemic heart disease, congestive cardiac failure, anaemia, diabetes, metabolic syndrome, obstructive sleep apnoea, osteoporosis, fractures and depression (Patel & Hurst, 2011). Whilst is goes beyond the scope of this thesis to discuss these in detail, the challenges of assessing and managing this complex multisystem disease are evident, with the progression of the disease and its co-morbidities not being fully understood. It is however conceivable that some of these co-morbidities may themselves adversely affect pulmonary function, especially when viewing the respiratory system in a wider context, including the lungs and surrounding musculoskeletal structures. For example collagen degradation or vertebral fractures, which are prevalent in COPD, are detrimental to pulmonary function because of pain and thoracic cage restriction (Patel & Hurst, 2011). Likewise hyperinflation results in the ribs adopting a more horizontal orientation, which in turn may contribute to chest wall rigidity and impair inspiratory muscle action (Courtney, 2009). Further consideration of this will be discussed later in the thesis.

1.2. Management of COPD

Over the last few years a range of management guidelines have been developed to assist the early diagnosis of COPD and to facilitate implementation of evidence-based multidisciplinary care for management (American Thoracic Society, 2004; NICE, 2004; 2010; GOLD, 2010; 2011). Whilst it is beyond the scope of this thesis to consider these individually, it is relevant to mention the Global Initiative for Chronic Obstructive Lung Disease (GOLD), which fosters

collaboration between experts and those working in this specialist area across the world. Each year GOLD revises their guidelines based on current empirical evidence to expedite early implementation of best available empirical evidence into management and clinical practice (GOLD, 2010; 2011). Whilst the 2011 Guidelines (GOLD, 2011) continue to have a focus on early, accurate diagnosis, reduced exposure to risk factors, dissemination of guidelines and integrative or multidisciplinary care, this document broadens focus to consider co-morbidities and extra-pulmonary features of COPD. Acknowledgement that a range of co-morbidities, such as osteoporosis, cardiometabolic disease, anxiety and depression may play an important part in the management of COPD, reflects the need to consider COPD as a multisystem disease (GOLD, 2011).

Evidence-based non-pharmacological management of stable COPD is currently limited to smoking cessation and multimodal pulmonary rehabilitation (GOLD, 2011). Pulmonary rehabilitation is a multidisciplinary management approach that combines physical exercise training with education and psychosocial support, with physical exercise considered the most beneficial element (ATS/ERS, 2006; GOLD, 2011). Physical exercise training as an intervention broadly comprises of three types of exercise, 'flexibility, aerobic and anaerobic exercises' (National Heart, Lung, and Blood Institute, 2007). Generally, physical exercise in pulmonary rehabilitation is focused on developing 'cardiovascular fitness' or physiological capacity through aerobic exercise, such as stair climbing or walking, rather than 'flexibility'. A number of authors have postulated that interventions aimed at increasing chest wall flexibility through active therapeutic exercise or passive hands-on manual therapy may be beneficial in COPD management (Miller, 1975; Masarsky & Weber, 1988; Hondras *et al.,* 2005; Putt *et al.,* 2008; Noll *et al.,* 2009). The rationale being such interventions may reduce the work of breathing by facilitating respiratory biomechanics. In order to appreciate the contribution that biomechanics may make to respiratory function it is important to firstly review the regional anatomy.

1.3. Anatomy and respiratory biomechanics

The anatomy in the thoracic region is complex with the thoracic cage, a bony and cartilaginous structure surrounding the thoracic cavity, appropriately designed to offer protection for vital organs. Whilst affording protection to the heart and lungs it also allows some movement linked to the respiratory cycle. In the next section a brief overview of the skeletal and muscular anatomy is provided leading to a description of respiratory biomechanics

1.3.1. Skeletal anatomy

The skeletal anatomy of the thoracic region comprises 12 thoracic vertebrae, 12 sets of ribs, 2 clavicles and the sternum (see Figure 1). The clavicle is often considered an accessory structure of the thoracic cage given its insertion to the manubrium and cartilage of the 1st rib.

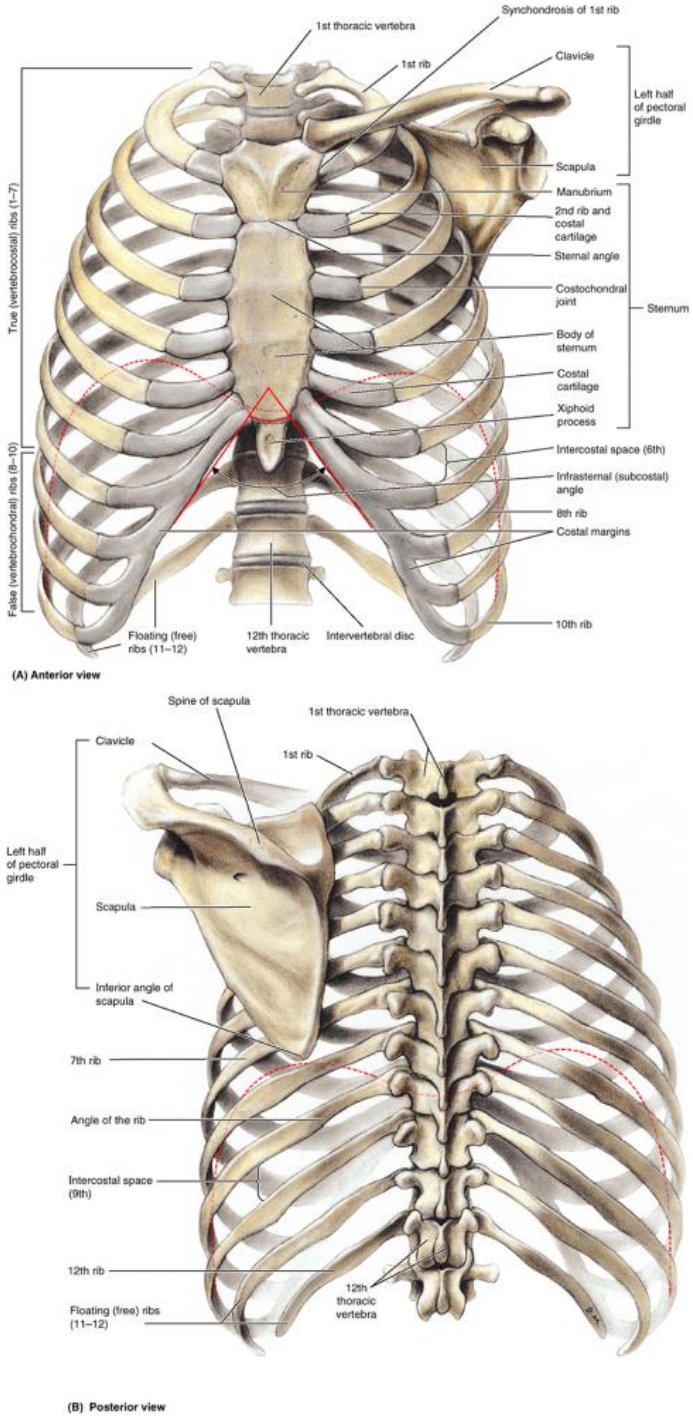


Figure 1. Anterior and posterior view of thoracic rib cage (http://dermatologic.com.ar/1.htm)

As well as the articulations between each thoracic vertebra, each rib (typically) has two facets; one for articulation with the corresponding vertebrae via the transverse process

(costotransverse joint) and one for articulation with the immediately superior vertebrae (costovertebral joint): see figure 2. Anteriorally the ribs (1-10) attach directly or indirectly to the sternum.

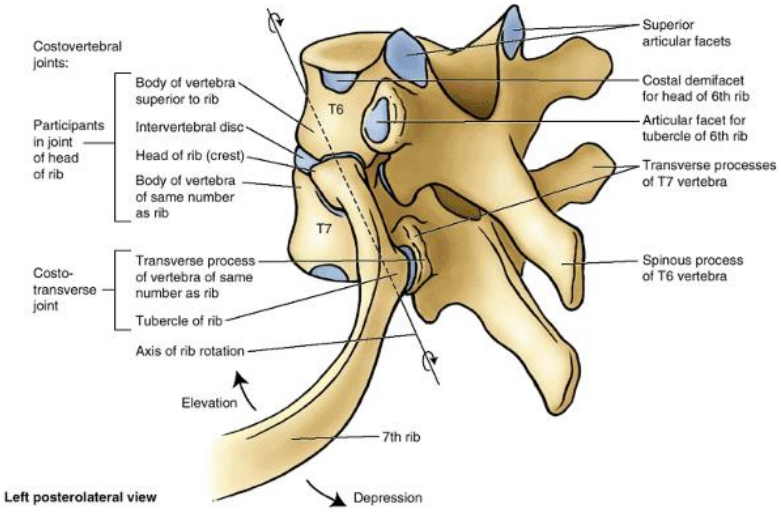


Figure 2. Posterolateral view of thoracic vertebrae and rib (http://dermatologic.com.ar/1.htm)

There are three groupings of ribs, the upper seven (true ribs) are attached to the sternum by means of costal cartilage with their elasticity allowing movement during the respiratory cycle. The 8th, 9th, and 10th ribs (false ribs) join with the costal cartilages of the ribs above. The 11th and 12th ribs (floating ribs) are such that they do not have any anterior connection to the sternum. Appendix 1 provides a summary of all the articulations in the thoracic cage.

1.3.2. Respiratory muscles and posture

There are over 112 muscles with attachments directly or indirectly to the thoracic rib cage and through their anatomical relations likely have a role in supporting respiratory function to a lesser or greater extent, and under normal or abnormal conditions (see appendix 2). Figure 3 illustrates the main muscles associated with the respiratory cycle. Inspiration is an active process, mainly involving contraction of the diaphragm, whilst expiration is entirely passive

under normal conditions. In COPD expiration becomes active with airflow obstruction, support coming from abdominal muscles, see section 1.4.2. Support for inspiration, under pathological conditions such as COPD, is provided by accessory respiratory muscles (sternocleidomastoid, scalenes, pectoralis minor and upper trapezius muscles) and may lead to postural changes that can be observed clinically. These include a forward head posture with protracted and elevated shoulder girdles (Chaitow 2002). A forward head posture is also often adopted to open the upper airways (Courtney, 2009). Whilst secondary or beneficial for ventilation in the short term, these musculoskeletal adaptations may alter head, neck, jaw and shoulder biomechanics, resulting in musculoskeletal pathologies and pain (Courtney, 2009). It is therefore conceivable that these changes may themselves adversely affect respiratory function.

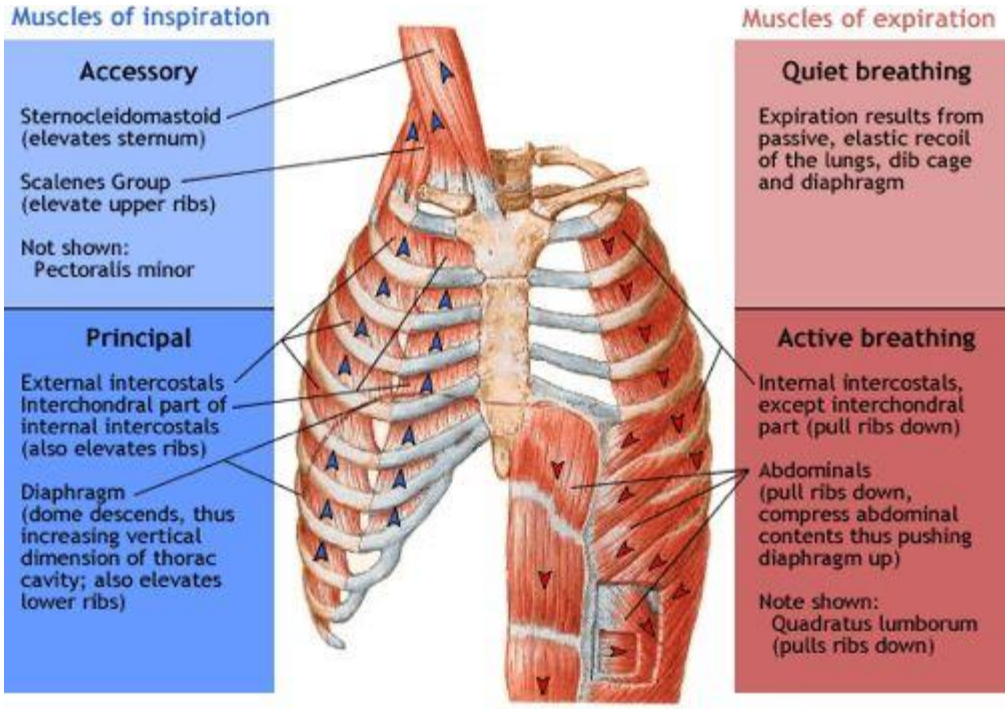


Figure 3: Muscle of respiration (http://soundersleep.com/musclesOfRespiration.php)

Respiratory function is widely understood to be controlled by the complex interaction of anatomical, biochemical and physiological reflexes (Dong *et al.,* 2009). Whilst advances in

medical research have only recently enhanced our understanding of the latter two of these, accounts detailing respiratory joint biomechanics date back nearly 2000 years. Galen, a Roman physician first described the upward movement of the ribs as the mechanism by which air moves through the lungs back in AD 138-210 (Jordanoglou, 1995).

1.3.3. Respiratory joint biomechanics and pulmonary dysfunction

During inspiration the lateral dimensions of the thoracic cavity are increased with the 7-10th ribs moving laterally (akin to bucket handles). The anteroposterior dimension is increased by the sternum being pushed forward and upward by the true ribs (1-6) likened to pump handles. For the 11th and 12th floating ribs that have no costotransverse attachment the motion produced is described as 'calliper' like, occurring along a horizontal plane. The direction of the rib motion is predominantly determined by the orientation and shape of the facets on the head of the ribs and the corresponding costal facets of the vertebrae (Williams, 1995).

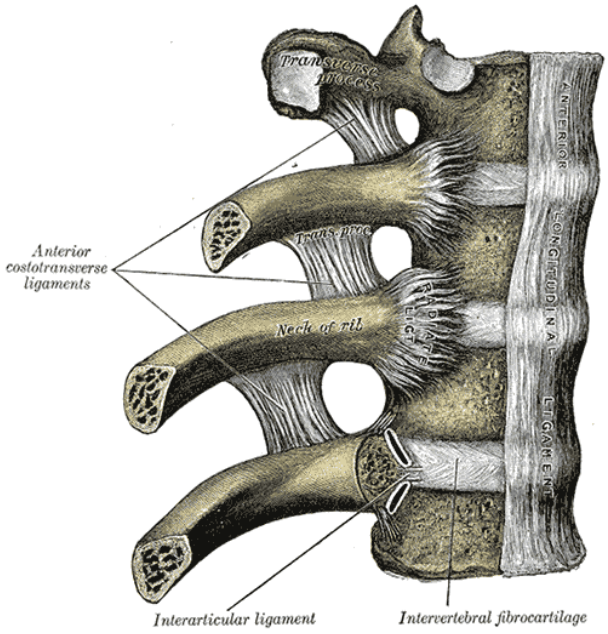


Figure 4. Costovertebral joint anatomy in the mid thoracic spine (http://www.mananatomy.com/body-systems/skeletal-system/joints-rib-cage)

The thoracic spine provides support posteriorly, and an anchorage for the ribs, thus facilitating respiration in healthy subjects. See Figure 4. With the ribs being inextricably linked to the thoracic spine via the costovertebral and costotransverse joints, it is theoretically conceivable that abnormalities in spinal motion or posture may exert some influence on pulmonary function. Although in theory it appears reasonable to suppose that changes to musculoskeletal structures such as bones, joints, posture and muscles in the thoracic region have the potential to influence pulmonary function through mechanical alterations, little attention has been given to evaluating this. Most of what is known of this relationship has emerged from research demonstrating reduced pulmonary function in idiopathic spinal scoliosis (Leong *et al.,* 1999) and osteoporosis (Harrison *et al.,* 2007). Leong *et al.,* (1999) investigated spinal stiffness and compared chest cage motion in healthy individuals compared to those with scoliosis (age 10-20 years) during a deep breath using skin sensors and motion analysis. They concluded that spinal stiffness contributes to pulmonary dysfunction, with structural abnormalities leading to reduced lung volume, impaired rib movement and altered respiratory muscle mechanics.

Harrison *et al.,* (2007) concluded from a systematic review of four case control studies (total sample n=109) that osteoporosis-related kyphosis (secondary to vertebral fractures) was associated with impairment of pulmonary function. Furthermore the pulmonary dysfunction, (reduced vital capacity, FEV_1, FVC, total lung capacity) appeared to be related to the number of spinal vertebral fractures and clinical measures of kyphosis. The study which was considered highest quality (blinded and with a population of non-smokers) found a moderately strong negative association between kyphosis angle and FEV_1 ($r=-0.713$, $p<0.05$). However the study had limited external validity because it consisted of only females recruited from specialist clinics and there was no a priori determination of sample size. Whilst further research with larger mixed samples is required, this provides suggestive evidence of pulmonary dysfunction secondary to structural disturbance of the thoracic cage.

A further example of altered respiratory biomechanics and pulmonary dysfunction is evident in older adults, where a reduction in total lung capacity is apparent. Whilst multifactorial in nature, with reduced numbers of elastic fibres in the lung tissue and a reduction in central nervous system respiratory drive partly contributing to the altered lung function, musculoskeletal changes, including changes affecting the rib cage, are also highly prevalent. These include costal cartilage calcification; costovertebral joint degeneration and decrease in intervertebral space with disc degeneration or respiratory muscle fibre changes (Nathan et al., 1964; Edmondston & Singer, 1997; Britto *et al.,* 2009). Collectively these changes in the musculoskeletal system may limit lung expansion or partly explain the observed reduction in total lung capacity seen in older adults (Scarlata, 2012), widely referred to as a 'restrictive' pulmonary disorder. This is in contrast to the airflow obstruction found in COPD, where reduced airflow secondary to swelling and inflammation in the airways is the main pathophysiological feature. The nature of pulmonary dysfunction associated with obstructive and restrictive disorders therefore differs, with clinical diagnosis currently being made primarily from pulmonary function testing and summarised in table 1.

Table 1. Characteristics of obstructive and restrictive lung disease

	Obstructive	Restrictive
Characteristics	Reduced airflow due to inflammation and swelling in airways. Results in high residual volume of air at full exhalation (hyperinflation)	Reduced total lung capacity Lungs are restricted from fully expanding for a number of reasons
Examples	COPD Asthma Bronchiectasis Bronchiolitis	Classification of types 1. Intrinsic- applies to lung disorder (pneumonia, tuberculosis) **2. Extrinsic – relating to outside anatomical border of lungs (scoliosis, chest wall deformity, rib fractures, obesity)** 3. Neurological – resulting from neurological conditions (paralysis of diaphragm, muscular dystrophy)
FVC	Decreased or normal	Decreased
FEV_1	Decreased	Decreased or normal
FEV_1/FVC	Decreased	Normal or increased
Total lung capacity	Normal or increased	Decreased

Although restrictive and obstructive lung disease may co-exist, COPD is by current definition primarily a disease of obstruction. This may be partly due to difficulties in establishing a clear diagnosis of restrictive lung disease, given flow-volume curves are insufficient and techniques to accurately measure lung volume, such as plethysmography are required (Goldman *et al.,* 2005). Moreover restrictive lung disease is much less clearly defined, being an umbrella term to include several diseases, including the lung (intrinsic) and non-respiratory diseases which secondarily impair pulmonary function (extrinsic or neurological). Scarlata *et al.,* (2012) provide an exhaustive list of diseases which may cause a restrictive pattern of pulmonary function, ranging from central neurological diseases to musculoskeletal disorders such as ankylosing spondylitis.

Their interest in this relates primarily to the increased prevalence of such conditions in older adults (11.1% in subjects >75 years, compared to 6.2% among subjects 17-44 years) and investigating the diagnostic and prognostic values of restrictive pulmonary impairment. It would therefore seem reasonable to hypothesise that pulmonary dysfunction in subjects with COPD may be both restrictive and obstructive in nature. This is partly due to the higher prevalence of conditions that predispose to restrictive lung disease with increasing age, and partly due to evidence of skeletal abnormalities in patients with COPD, analogous to those found in ankylosing spondylitis. These include changes to bone (Jorgensen *et al.,* 2007) and vertebral body morphology (Kjensli *et al.,* 2009) In a sample of 462 people with COPD (mean age 63 years, range 32-83 years) and control (age 65 years, range 50-80 years) vertebral body deformities were identified in 31% of COPD group compared to just 18% of the control group (Kjensli *et al.,* 2009). Jorgensen *et al.,* (2007) also reported changes in bone in a relatively small cross sectional study (n=62) of 50-70 year old COPD subjects, whereby 68% of the sample were diagnosed as having osteoporosis or osteopenia (n=22 and 16 respectively).

Whilst the above is a review of changes in COPD with respect to bone, the following section details evidence of other musculoskeletal changes, beyond bone, in the cervico-thoracic region of subjects with COPD.

1.4. Musculoskeletal changes in COPD

There are a plethora of studies investigating bone mineral density, skeletal muscle physiology and function (strength, endurance) in COPD, although interestingly, there is little research into bony form and function, such as spine posture and range of motion. This is not surprising, as its name suggests it is a disease defined by airflow obstruction. However respiratory textbooks often describe postural changes, muscle length changes, osteoporosis *etc*. all of which could, as described for ankylosing spondylitis lead to pulmonary dysfunction of a restrictive nature. A few studies have compared COPD patients with healthy subjects across a range of musculoskeletal

structures, although no definitive conclusions could be drawn due to the paucity, methodological quality and heterogeneity of the studies. Having previously referred to some of the literature concerning bony changes (Jorgensen *et al.,* 2007; Kjensli *et al.,* 2009), the following section describes the evidence in relation to the thoracic cage and accessory muscles of respiration in COPD. Appendix 3 provides more comprehensive information on studies described below. This evidence was subsequently used to inform the scope of performance-based measures used in final study of this thesis, differences in the cervico-thoracic musculoskeletal system in subjects with COPD: a case control study (Chapter 5).

1.4.1. Thoracic cage

Structural differences in the rib cage configuration, which as mentioned previously could influence respiratory biomechanics, have been investigated in relation to the presence of hyperinflation in COPD (Walsh *et al.,* 1992; Cassart *et al.,* 1996). Walsh *et al.* (1992), using radiographic images, concluded that, whilst the diaphragm position was significantly lower in COPD (n=10) compared to age matched controls (n=10), and may affect the available range of diaphragmatic muscle excursion, bony configuration was similar compared to a matched healthy group. Cassart *et al.,* (1996; abstract only) however performed a similar study using computerised tomography in a sample of COPD subjects (n=7) with severely impaired pulmonary function (FEV_1 25±7% predicted), and reported an increase in anterior-posterior measurements for all lung volumes, which was not evident in the transverse plane. They concluded that the marked hyperinflation seen in COPD does produce complex changes to rib cage dimensions which have implications for respiratory muscle length and function. Kasai *et al.,* (2003) concluded that such changes were also likely progressive and associated with disease severity. They found thoracic cage cross-sectional area, measured using computerised tomography correlated well with total lung capacity $r=0.62$, $p<0.005$), functional residual capacity ($r=0.67$, $p<0.001$) and residual volume ($r=0.62$, $p<0.005$) and indicative of

hyperinflation. And that classification using Fletcher's 5-point dyspnoea scale correlated statistically significantly with a ratio of thoracic cage measures (total cross sectional area and height) supporting the idea that dyspnoea and chest wall structure are related.

Whilst these studies differ considerably in methodology and present mixed findings, they do lend preliminary support to the idea that rib cage configuration differs in COPD and is likely related to disease severity, associated with hyperinflation. The generalisability to less severe presentations is therefore limited. Furthermore the clinical relevance of such changes however remains unclear.

1.4.2. Muscle

Whilst there are many studies that have explored changes to muscle in COPD, the focus has been on the respiratory muscles such as internal/external intercostal muscles and diaphragm (Orozco-Levi, 2003; Duiverman *et al.,* 2009), peripheral muscle strength (Ansari *et al.,* 2007; Vilaro *et al.,* 2009) and abdominal muscle involvement (Ninane *et al.,* 1992). Less research has been done on accessory muscles of respiration *e.g.* sternocleidomastoid, trapezius, pectoralis, scalene, and spinal muscles *e.g.* semispinalis or erector spinae. Furthermore, the primary focus for much of this work has been in relation to skeletal muscle physiological function, frequently studying a few muscles in isolation, and often with small and poorly described samples. For example, Loukas *et al.* (2008) measured muscle characteristics of the serratus posterior superior and inferior muscles in order to evaluate possible functionality as a respiratory muscle based on its anatomical location. Using a sample of cadavers (n=50, age range 58-82) where eighteen had a history of COPD no statistically significant ($p>0.05$) differences were found in their length, thickness and width suggesting they have no role respiration. These muscles are however rarely cited as being primary muscles of respiration, making it difficult to relate to other work or infer any clinical relevance. Additionally, the finding from *in vitro* studies, where

pulmonary function cannot be evaluated, adds little to our knowledge and understanding of respiratory biomechanics of this muscle in isolation.

Sternocleidomastoid (SCM) has received greater research attention, with a number of studies investigating its length, strength, function in COPD patients (De Troyer *et al.,* 1994; Gandevia *et al.,* 1996; Peche *et al.,* 1996; de Andrade *et al.,* 2005). In summary, it appears SCM has little role in respiration at rest for patients with COPD of differing severities (De Troyer *et al.,* 1994; Gandevia *et al.,* 1996), however it does appear to have a role where resistance to breathing is increased as demonstrated in studies using inspiratory muscle training devices (de Andrade *et al.,* 2005). In a study of seven healthy elderly subjects, mean age of 68 ± 4 years and seven COPD patients, FEV_1 45 ± 17%, with mean age 66 ± 8 years activity of SCM was found to negatively correlate with the level of obstruction (r = −0.537) (de Andrade *et al.* 2005). With respect to structural change, SCM appears to have an increased cross-sectional area in COPD (4.29 ± 1.48 cm^2) compared to 3.96 cm^2 in the control group, however the torque was found to be similar to the matched controls, once adjustment for length was made (Peche *et al.,* 1996). Most of these four studies used relatively small samples ranging from n=7 to n=40. The heterogeneity with respect to disease severity and measurement tools (needle and surface electromyography and computerised tomography, dynamometry) limit any firm conclusions being made about the role and function of this one neck muscle in COPD respiratory biomechanics. However, overall, the results are not unsurprising given its role as accessory muscle to respiration and principally being recruited where work of breathing may increase.

The scalene muscles, which attach to the upper two ribs have also been found to have a role in respiration, with levels of activation being reported in COPD subjects (n=40) during quiet breathing in sitting and supine (De Troyer *et al.,* 1994). Using ultrasound guided needle EMG, Gandevia *et al.* (1996) reported heightened levels of muscle activity, measured via discharge frequencies of single motor units, in the scalene ($p<0.02$) and second parasternal intercostal

($p<0.05$) muscles of seven patients with stable COPD (FEV1 33±13% predicted) and seven matched control subjects. A limitation of this research principally relates to very small sample size (n=7) and the reported discomfort experienced during needle placement potentially affecting levels of motor unit firing. Moreover Duiverman *et al.,* (2009) concluded from a larger study (COPD n=17, healthy subjects n=10) that scalene activity increased almost immediately after onset exercise, whereas in controls onset of scalene activity was evident later on in the exercise testing.

The role of the abdominal muscles has been investigated by Ninane *et al.* (1992), who concluded that transverse abdominis muscle activity, using ultrasound guided needle electromyography, was related ($p<0.005$) to the level of pulmonary function during quiet breathing in subjects with severe airflow limitation. The rectus abdominis and external abdominis oblique muscles, however, were electrically silent. These are large expansive muscles, and, whilst the technique would ensure the target muscle was studied, it is questionable whether sufficient muscles fibres were tested to provide substantive evidence of activity across the whole muscle using this approach.

Although inconclusive due to the lack of high quality evidence this provides some evidence of changes in the cervico-thoracic region in COPD compared to healthy subjects and as such could be indicative of co-existing restrictive pulmonary disease of an extrinsic nature. Although there is much still be understood, it would appear reasonable that interventions aimed at improving chest wall flexibility may be beneficial for subjects with COPD. Manual therapy, including spinal manipulative therapy or mobility exercises targeting musculoskeletal structures of the thoracic region have been used in COPD management, the theory being increased thoracic cage flexibility would reduce the work of breathing. In fact Engel & Vemulpad (2009) take this idea further, proposing that such interventions may even impede the rate of disease progression if treated in mild to moderate stages of the disease. However this has not yet been substantiated.

1.5. Therapeutic interventions to aid flexibility and chest wall mobility

Musculoskeletal flexibility may be developed or maintained with active interventions, such as therapeutic exercise or stretching techniques (muscle or joint) (Page, 2012), or passive therapies, such as massage or mobilisation techniques (Hopper *et al.,* 2005). Whilst much research into flexibility has been done in younger subjects and in peripheral joints (knees, hips), two studies were found that investigated the effectiveness of spinal flexibility exercises for older adults. An increase in spinal range of motion in the sagittal plane was reported in a sample of older adults (n=20, aged 71-78 years) doing a l0-week flexibility programme (Rider & Daly, 1991) and Katzman *et al.,* (2007) reported a statistically significant reduction in spinal kyphosis (−6°±3°) and best kyphosis (−5°±3°) ($p<0.001$)] following a 12-week group exercise programme in older women (n=21, aged 72.0±4.2 years, with spinal kyphosis of more than 50-degrees). These findings lend some support for trials of flexibility training as a means of increasing spinal mobility and improving posture in older adults.

There is a paucity of musculoskeletal research in the thoracic spine, which is likely a consequence of its anatomical complexity and lower reported prevalence rates of dysfunction compared with the cervical and lumbar regions. In terms of the relationship between the thoracic spine and pulmonary function in respiratory disease, this could be attributed to a bias towards physiology-based research, but also to gaps in our understanding of the relationship between the musculoskeletal system and pulmonary function. Interestingly, this gap in the evidence base is acknowledged in the physiotherapy literature with recent physiotherapy guidelines recommending research into the effect of thoracic mobility exercises, an active therapeutic intervention in COPD (Bott *et al.,* 2009).

Although thoracic mobility exercises *per se* in COPD have not yet been systematically evaluated, research into other active and passive therapeutic approaches targeting musculoskeletal structures (joints, muscle, connective tissues), and aimed at improving respiratory biomechanics

have been published, namely respiratory muscle stretch gymnastics (RMSG), manual therapy and more recently Tai Chi. Although studies of Tai Chi in COPD have produced some favourable results with respect to lung function and exacerbation rates (Chan *et al.,* 2011), the combination of exercise with meditation focused on breathing limits its direct relevance to this thesis. Therefore, Tai Chi as a discrete intervention will not be considered any further.

1.5.1. Respiratory muscle stretch gymnastics

RMSG comprise a series of five therapeutic active exercises or *'patterns'* of movement in the thoracic region with the aim of reducing dyspnoea through increased chest wall flexibility (Ito *et al.,*1999; Kakizaki *et al.,* 1999; Minoguchi *et al.,* 2002) (see Table 2). The programme, whilst targeting skeletal muscle, differs from inspiratory muscle training, which aims to increase respiratory muscle endurance and strength, rather than the flexibility of all muscles directly or indirectly related to respiration (Minoguchi *et al.,* 2002).

Although the RMSG studies used small sample sizes (n=12 for each), these small pre-post (Yamada *et al.,* 1996) and randomised controlled trial (Minoguchi *et al.,* 2002) demonstrate that RMSG may afford some therapeutic benefit in COPD management. The active interventions used in the studies required participants to undertake RMSG three (Yamada *et al.,* 1996) or four times (Minoguchi *et al.,* 2002) a day over a four-week period. Performance-based measures, including the six-minute walking test, improved significantly with RMSG, with studies reporting a statistically significant increase in distance covered (383±24 m to 430±16 m) compared to inspiratory muscle training (386±21 m to 412±18 m), p=0.04 (Minoguchi *et al.,* 2002) or 43±30 m increase in distance post intervention ($p<0.01$) (Yamada *et al.,* 1996). Minoguchi *et al.* (2002), using a crossover study design to compare RMSG to inspiratory muscle training, found that the former resulted in better six-minute walking test results compared to inspiratory muscle training (p=-0.001). Patient-reported measures of effect also improved with a reduction in dyspnoea at the end of the six-minute walk (on a 15 cm visual analogue scale 5.0±1.2 cm to

4.3±1.3 cm (Minoguchi *et al.,* 2002) and from 6.5±4.1 to 3.6±3.7, $p < 0.05$ (Yamada *et al.,* 1996). However this did not differ significantly from inspiratory muscle training (Minoguchi *et al.,* 2002). Improvements in quality of life were also reported for the RMSG intervention which used the Chronic Respiratory Disease Questionnaire, although details of the extent of change were unavailable (Japanese article) (Yamada *et al.,* 1996).

A more recent single case study in a mechanically ventilated COPD patient by Leelarungrayub *et al.,* (2009) also reported positive effects on chest wall expansion and dyspnoea using an intervention of chest wall stretching exercises. Although collectively these studies provides some preliminary evidence that RMSG or flexibility exercises may afford some therapeutic benefit in COPD management, a larger clinical trial is required prior to RMSG being accepted as a viable alternative management intervention for COPD.

Table 2. Respiratory Muscle Stretch Gymnastics Programme

Respiratory Muscle Stretch Gymnastics

Patients perform the stretch patterns in order 4 times a day.

'Pattern 1. Elevating and pulling back the shoulders
As you slowly breath in through your nose, gradually elevate and pull back both shoulders. After taking a deep breath, slowly breathe out through your mouth, relax and lower your shoulders.

Pattern 2. Stretching the upper chest
Place both hands on your upper chest. Pull back your elbows and pull down your chest while lifting your chin and inhaling a deep breathe through your nose. Expire slowly through your mouth and relax.

Pattern 3. Stretching the back muscle
Hold your hands in front of your chest. As you slowly breathe in through your nose, move your hands front wards and down, and stretch your back. After deep inspiration, slowly breathe out and resume the original position.

Pattern 4. Stretching the lower chest
Hold the ends of a towel with both hands outstretched at shoulder height. After taking a deep breath, move your arms up while breathing out slowly. After deep expiration, lower your hands and breathe normally.

Pattern 5. Elevating the elbow
Hold one hand behind your head. Take a deep breath through your nose. While slowly exhaling through your mouth, stretch your trunk by raising your elbow as high as is easily possible. Return to the original position while breathing normally. Repeat the process using the alternate hand behind the head.'

(Minoguchi *et al.,* 2002)

1.5.2. Manual Therapy

Manual Therapy is:

> *'A clinical approach utilizing skilled, specific hands-on techniques, including but not limited to manipulation/mobilization, used by the physical therapist to diagnose and treat soft tissues and joint structures for the purpose of modulating pain; increasing range of motion; reducing or eliminating soft tissue inflammation; inducing relaxation; improving contractile and non-contractile tissue repair, extensibility, and/or stability; facilitating movement; and improving function'* (AAOMPT, 1999; APTA, 2011).

Manual therapy is core to the osteopathic, chiropractic and manipulative physiotherapy professions, with management interventions being, in the main, passive, delivered through a range of hands-on approaches, such as spinal manipulative techniques, massage or stretching of tissues. Whilst all physiotherapists have some training in these techniques, manipulative physiotherapy, also known as manual therapy, is considered specialist practice and clinicians may well have undertaken postgraduate training to acquire advanced therapeutic skills for the management of patients; the patient population that these physiotherapists manage present primarily with complaints originating in the musculoskeletal system (IFOMPT, 2012).

The focus of manual therapy research extends beyond the neuromusculoskeletal system, although this has come predominantly from the osteopathic and chiropractic professions. In terms of manual therapy as a management approach in respiratory disease, there is a small but relevant body of evidence in relation to asthma care (Hondras *et al.,* 2005; Ernst, 2009), cystic fibrosis (Massery, 2005) and COPD (Miller *et al.,* 1975; Witt & MacKinnon, 1986; Masarsky & Weber, 1988; Beekan *et al.,* 1998; Noll *et al.,* 2008; 2009; Dougherty *et al.,* 2011). The proposed rationale for all studies evaluating manual therapy and respiratory disease is founded on the notion that there is a relationship between the function of the musculoskeletal system,

specifically flexibility in the thoracic cage, and pulmonary function. Two independent systematic reviews (Hondras *et al.,* 2005; Ernst, 2009), including a Cochrane review of manual therapy for asthma (Hondras *et al*, 2005), concluded there was insufficient evidence to support manual therapy as a management approach in asthma care. The pathophysiology of asthma is different to COPD, with airflow variability in asthma being evident over shorter periods and inflammation associated with exposure to an allergen or irritant. In view of this and given a number of studies of manual therapy in COPD populations were identified, an evidence synthesis was therefore required as part of this thesis. A systematic review of manual therapy in COPD therefore forms the focus of Chapter 2 of this thesis. Due to the paucity of evidence of other relevant areas of research, a narrative review of evidence for manual therapy as a means of increasing joint mobility is detailed below.

Evidence for manual therapy as an intervention for increasing joint mobility

Research into the clinical effectiveness of manual therapy as a passive therapeutic management approach is generally focused on the management of symptomatic dysfunction in musculoskeletal tissue, mainly focused on pain rather than as a means of enhancing joint mobility or flexibility. A database search of the available empirical evidence into the effectiveness of manual therapy as a therapeutic intervention to increase joint mobility identified many studies but predominantly with a focus on pain or other musculoskeletal symptoms. This is unsurprising, given the driving force behind much of the research in musculoskeletal dysfunction is pain; patients are less likely to go to their GP complaining of stiffness or lack of flexibility as a primary complaint. To illustrate this, a recent best evidence synthesis concluded that spinal manipulation/mobilisation, a specific form of manual therapy, is effective for acute, sub-acute and chronic low back pain, migraine and cervicogenic headache, cervicogenic dizziness and acute/sub-acute neck pain (Bronfort *et al.,* 2010). Pain was the

primary patient reported outcome measure in these studies, with no mention of flexibility or joint mobility.

Research into the effectiveness of manual therapy as a means of increasing spinal joint mobility or flexibility in asymptomatic subjects, or those with sub-clinical presentations, is lacking in humans, and the evidence found from equine studies has no external validity to humans (Haussler *et al.,* 2007; Haussler *et al.,* 2010). One recent study in humans (n=35, mean age 21± 4 years) did find significant increases in neck motion [cervical flexion: mean change in degrees (95% confidence interval) of 2.5 (0.0 to 5.0) 2 compared to -2.2 (-5.7 to 1.4) in the control group (p= 0.03), extension: 4.9 (1.8 to 7.9) compared to -1.2 (-8.1 to 5.6) in the control group (p=0.045)] following '*Cervical Myofascial Induction*', a form of soft tissue manipulation to the ligamentum nuchae, a ligament in the posterior cervical spine (Saíz-Llamosas *et al.,* 2009). However none of the results exceeded the minimum clinically importance difference which is 18.8 degrees for flexion, 13 degrees for extension (Cleland *et al.,* 2006). Whilst the effects on lateral flexion and axial rotation were less favourable (see table 3), it is reasonable to conclude that manual therapy techniques need to be specific and directed at a clinically diagnosed dysfunctional musculoskeletal structure.

Table 3: Changes in neck mobility (mean with associated 95% confidence interval)

Movement	**Experimental group (n=19)** **Mean (degrees)** **(95% confidence interval)**	**Control group (n=16)** **Mean (degrees)** **(95% confidence interval)**	**MCID** **Mean**
Cervical right lateral flexion	1.1 (-1.2 to 3.4)	-1.5 (-4.5 to 1.2)	10
Cervical left lateral flexion	3.2 (0.2 to 6.2)	-1.2 (-4.3 to 1.9)	19
Cervical right axial rotation	0.4 (-3.9 to 4.7)	-1.8 (-6.6 to 2.9)	13.9
Cervical left axial rotation	0.8 (-2.6 to 4.3)	1.1 (-4.5 to 6.7)	13.9

Given the ligamentum nuchae functions as a passive restraint for excessive cervical flexion, and exerts little effect on movement in the other planes, these results are therefore not surprising. With the use of a small sample, a therapeutic technique targeting young, healthy tissue (average age of participant 21 years) in an asymptomatic population, and failure to achieve the minimum clinically importance difference in all movements this study provides little robust evidence to support or refute a potential role for manual therapy in enhancing musculoskeletal flexibility in older adults with likely age-related tissue changes. The effectiveness of any intervention can only be determined using reliable and valid measures of mobility; in this study cervical rotation was measured using a goniometer which had been previously tested with intraclass correlation coefficients (ICC) ranging from 0.66 to 0.94 being reported (Saíz-Llamosas *et al.,* 2009). Measurement in the thoracic region is significantly more challenging given the anatomical complexity of the thoracic cage and relatively smaller ranges of motion.

1.6. Measurement of chest wall mobility

A small number of studies have attempted to quantify or describe chest wall motion either using a tape measure or skin sensors placed over the chest wall. Researchers used the difference in chest circumference, 'cirtometry' (three points: axillary, xiphisteral and abdominal levels) at the point of maximal inspiration and expiration as a measure of chest wall mobility in COPD (Putt *et al.,* 2008; Leelarungrayub *et al.,* 2009; Malaguti *et al.,* 2009). Malaguti *et al.,* (2009) reported within day intra and inter-rater reliability of 0.84-0.95 ($p<0.001$) and 0.69-0.89 ($p=0.004$) respectively in a sample of twenty-six male participants with COPD. Inspiratory capacity did not appear to be associated with axillary and xiphisternal mobility, although chest wall mobility at the abdominal level did show a positive relationship with inspiratory capacity ($r=0.4$, $p=0.04$). Putt *et al.,* (2008) used axillary and xiphisternal cirtometry pre and post a muscle stretching intervention in COPD (n=14) whilst Leelarungrayub *et al.,* (2009) used this approach to measure chest expansion in a single case study of a ventilated COPD patient.

Culham *et al.,* (1994) and Leong *et al.,* (1999) used skin sensors placed on the chest wall to investigate motion analysis in subjects with osteoporosis and healthy and idiopathic scoliosis respectively. Aside a number of methodological weaknesses neither study managed to overcome the fundamental issue with skin sensor based motion analysis systems, soft tissue artefact; movement occurring between skin and bone and/or skin and sensor (Willems, *et al.,* 1996). Soft tissue artefact is widely considered a significant source of measurement error (Andriacchi & Alexander, 2000) and, in lower limb motion analysis, has led to a diverse range of alternative approaches being evaluated (Leardini *et al.,* 2005). For lower limb kinematic research, the combination of motion analysis with imaging technology has led to improvements in the quality of the research (Patel *et al.,* 2004); a result of advances in imaging technology and an acknowledgement that other methodological approaches using skin sensors, do not fully compensate for this source of measurement error (Leardini *et al.,* 2005).

During the development of this thesis it was evident that existing or ideal measures of chest wall mobility were neither ethically feasible (exposure to ionising radiation) nor valid. As a result ultrasound imaging was utilised to investigate soft tissue artefact in the thoracic region as an accessible, safe and inexpensive alternative imaging tool. In the absence of published guidelines, ultrasound scanning of young healthy subjects was done with an experienced sonographer in order to identify distinct anatomical bony features of the antero-lateral thoracic cage. However this proved unsuccessful with the external surface of mid thoracic ribs being smooth and therefore impossible to acquire a clear reproducible image of a known landmark to facilitate repeated measures. Acquisition of a high-quality image of a thoracic vertebra was however possible, and had in fact been done previously by a number of researchers to measure static vertebral bone position in subjects with idiopathic scoliosis in a prone lying position, as a means of quantifying spinal curvature (Suzuki *et al*., 1989; Burwell *et al*., 1999; Kirby *et al*., 1999). This therefore prompted the idea that ultrasound imaging of vertebrae could be combined with motion analysis in a more functional position to measure mobility.

Having briefly detailed the anatomy of the thoracic vertebrae and corresponding ribs in section 1.3.3, it is highly relevant that coupled motion of the ribs and adjacent spinal vertebra occurs during axial rotation. It is understood from a synthesis of theoretical (Saumarez, 1986; Cropper, 1996), cadaveric (Panjabi *et al.,* 1981) and clinical evidence (Lee, 1993), that right axial vertebral rotation couples with posterior rotation of the ipsilateral or right rib. The upper vertebra pushes the superior aspect of the head of the right rib backward at the costovertebral joint, inducing a posterior rotation of the neck of the right rib (Lee, 1993); movement that is equivalent to 'bucket handle' rib motion described in respiratory texts.

Relative to chest wall motion analysis, the thoracic spine has been widely researched albeit from a musculoskeletal perspective, focused on rotation and with negligible appreciation for the coupled motion occurring at the costovertebral and costotransverse joints. It is however,

reasonable, based on the coupled motion, to consider that approaches used to measure thoracic rotation may be viable substitutes for measuring rib motion. Based on this idea and assuming optimal tissue health, full range of thoracic axial rotation in both directions is dependent on the ribs being able to rotate fully around a paracoronal axis, from a position of end range posterior rotation to a position of end range anterior rotation (ipsilateral to contralateral thoracic rotation) and vice versa. One could also suppose that any disorder of the musculoskeletal system (degenerative changes, rib cage deformation secondary to hyperinflation *etc.*) would likely disrupt respiratory biomechanics.

As will become clear in chapter 3, the majority of published measurement approaches used in the thoracic spine rely on skin sensors or surface measures and therefore are of questionable validity owing to soft tissue artefact. In order to move the thoracic spine motion analysis evidence base forward it was necessary to quantify this source of error and establish whether existing approaches using just skin sensors were suitable for use in the main study or whether, in line with other motion analysis studies, alternatives had to be considered, such as combining imaging with motion analysis (Leardini *et al.,* 2005). Chapter 3 therefore reports an investigation of soft tissue artefact in the thoracic region during axial rotation in a population of young healthy subjects. Having quantified significant soft tissue artefact in the thoracic spine (Heneghan *et al.,* 2010) all existing approaches were rendered inadequate and therefore steps were taken to develop a new approach which would provide a more convincing measure of motion analysis, with ultrasound imaging of the spinal vertebra combined with motion analysis.

Ideally all measurement approaches should be valid for the population it is to be used for. In this case the combined use of imaging to view the underlying bone with motion analysis would need to be measured against the gold standard, considered x-ray in this region (Willems *et al.,* 1996). However, performing a validity study was outside scope of this doctorate primarily due to ethical reasons. Notwithstanding this, establishing the stability of measures and intra-tester

reliability of this novel approach was feasible. This was again investigated in a sample of young healthy adults as the aim was to evaluate the stability of measures on one occasion and reliability of the tester on three separate occasions. Whilst this was not the target population for the doctorate, they were chosen for convenience (ease of performing repeated measures, ethical approval); to enable comparison of results with existing studies and to minimise the influence of confounding factors associated with aging, such as spinal degeneration or fatigue. These confounding factors may have compromised the study as the primary aim was to establish the author's reliability of the technique. Once stability of measures and intra-tester reliability had been investigated (Heneghan *et al.,* 2009) this approach was subsequently used as the measurement of choice to describe thoracic cage flexibility in subjects with COPD compared with a matched healthy control group. This study is then reported in chapter 5.

This thesis therefore comprises a series of studies forming individual chapters which have been informed by the existing literature in a number of different fields, respiratory, biomechanics and musculoskeletal. The overall aim of the doctorate was to describe changes in the cervico-thoracic musculoskeletal system in patients with COPD and explore a possible link between musculoskeletal changes and pulmonary function. An exploratory study was therefore undertaken to describe a number of cervico-thoracic musculoskeletal changes in COPD, with a secondary aim of exploring their relationship with pulmonary function. An evidence-informed evaluation could then be used to inform further research in this field focused on active thoracic flexibility exercises or specific passive manual therapy interventions. The study and its findings are presented in Chapter 5.

Therefore, this thesis sets out to provide a:

1. Systematic review of the available evidence for manual therapy as a management approach for COPD

2. Critical evaluation of motion analysis approaches in the thoracic region with a report of soft tissue artefact

3. Description of the development of a novel measurement approach for use in the thoracic spine and evaluation of stability of measures and intra-tester reliability

4. Describe changes in the cervico-thoracic musculoskeletal system in COPD, and their relationship with pulmonary function

Chapter 2. MANUAL THERAPY TECHNIQUES IN THE MANAGEMENT OF COPD

Publications and Presentations

1. Heneghan NR, Adab P, Balanos GM, Jordan RE. (2012) Manual therapy for chronic obstructive airways disease: A systematic review of current evidence. Manual Therapy. 17(6): 507-518 (Appendix 4)

2. Heneghan NR, Jordan RE, Adab P, Balanos GM. Manual therapy for chronic obstructive airways disease (COPD): a systematic review of current evidence. World Confederation of Physical Therapy conference, Amsterdam. July 2010 (Poster presentation).

3. Heneghan NR, Adab P, Balanos GM. Jordan RE. Manual therapy for chronic obstructive airways disease (COPD): a systematic review of current evidence. International Federation of Orthopaedic and Manipulative Physical Therapists, Quebec. October 2012 (Oral presentation).

2.1. Abstract

Purpose: To systematically review evidence for manual therapy in chronic obstructive pulmonary disease (COPD) management.

Relevance: COPD is an increasing global problem. Evidenced based non-pharmacological management approaches are limited. Evidence suggests MT may be beneficial therefore an evidence synthesis is required.

Methods: Systematic review methodology (informed by Cochrane & Centre for Reviews and Dissemination Guidelines). Using predefined protocol key databases were searched (to January 2012). Included articles were RCT or quasi experimental studies and included: (1) adults with COPD; (2) manual therapy intervention; (3) a control, sham or alternative manual therapy intervention; (4) physiological measure of lung function. Following screening, data extraction and risk of bias assessment was undertaken by two independent reviewers. Key authors, bibliographies and citations were also screened. Descriptive results were collated and tabulated. A risk of bias tool was devised for data synthesis. Pooling of data and meta-analysis was not possible due to study heterogeneity.

Results: From 3086 articles 24 full-text articles were evaluated. 7 studies were included (5 RCTs, 2 pre-post studies). Of all COPD subjects (n=131) interventions included; osteopathic manipulative therapy (OMT) (n=100), massage (n=5), muscle stretching (n=14), and passive movements (n=12). Of the 7 studies, 6 were evaluated as high/moderate or unclear risk of bias, with one OMT study (n=25) being evaluated as low risk of bias. In this study, pulmonary function (FEV1, FVC) changed minimally (<1.5%) ($p>0.05$) immediately following OMT techniques. Paradoxically patient self-reported measures (´improved health´ and ´breathing difficulty´) improved following OMT (66%) compared to control (43%).

Conclusions: There is insufficient evidence to support the use of manual therapy in COPD management. Future exploratory work is required, or trials using validated patient reported measures in conjunction with physiological outcome measures over a longer term follow up period.

Implications: Evidence for manual therapy in COPD management is lacking.

The aim of this chapter is to consider whether manual therapy, a passive therapeutic intervention, may be useful as an adjunctive management approach in COPD and provide an evidence synthesis of the research into the effectiveness of manual therapy on COPD.

2.2. Introduction

Whilst primarily a disease of the pulmonary system, COPD has recently had its definition revised to take account of the high frequency of extra pulmonary co-morbidities; '*A preventable and treatable disease with some significant extra-pulmonary effects that may contribute to the severity in individual patients.....*' (GOLD, 2010). Furthermore, these extra pulmonary impairments appear to contribute significantly to overall disability associated with COPD (Eisner *et al.,* 2011).

Extra pulmonary features include cardiometabolic, musculoskeletal and psychological conditions. Two of the most prevalent co-morbidities include reduced bone mineral density (50-70%) and skeletal muscle dysfunction (32%) (Patel & Hurst, 2011). Skeletal muscle dysfunction is reported in respiratory and peripheral muscles with studies reporting reduced muscle strength (particularly quadriceps), poor muscle endurance and muscle fibre atrophy (DeTroyer *et al.,* 1994; Gandevia *et al.,* 1996; Orozco-Levi, 2003; Ansari *et al.,* 2007; Vilaro *et al.,* 2009).

As well as reduced bone mineral density (Jergenson *et al.,* 2007) and an increased prevalence of vertebral deformities (Kjensli *et al.,* 2009), structural differences in rib cage configuration have been reported in studies comparing COPD with matched controls (Kasai *et al.,* 2003).

Whilst dyspnoea is the main symptomatic feature of COPD, cervico-thoracic pain has also been recently reported in this patient population (Lohne *et al.,* 2010), perhaps as a consequence of musculoskeletal structure changes and dysfunction. Recent work by Bentsen *et al.,* (2011) reported that prevalence of pain (predominantly in the neck, shoulders and chest), a common

feature of musculoskeletal conditions, was notably higher in patients with COPD (45%) compared to the general population (34%). This is unsurprising given the observed use of accessory respiratory muscles in COPD relating to dyspnoea (Lohne *et al.,* 2010; Bentsen *et al.,* 2011) and the highly prevalent adoption of a forward neck posture. Interestingly though, many of the COPD subjects (n=45) reported using transcutaneous electrical nerve stimulation/acupuncture (n=14) to assist in pain management as opposed to other forms of physiotherapy, such as manual therapy or therapeutic exercise (n=7).

There are a number of published studies describing the use of manual therapy techniques for the management of COPD, predominantly from the osteopathic and chiropractic literature (Howell *et al.,* 1975; Miller *et al.,* 1975; Witt & MacKinnon, 1986; Masarsky & Weber, 1988; Noll *et al.,* 2008; 2009; Dougherty *et al.,* 2011). Advocates of manual therapy propose that passive techniques, aimed at increasing thoracic mobility, may work to reduce the work of breathing through enhanced oxygen transport and lymphatic return (Miller, 1975; Masarsky & Weber, 1988; Hondras *et al.,* 2005; Putt *et al.,* 2008; Noll *et al.,* 2009).

Whilst this theory has not been investigated in a COPD population, a myofascial release technique did affect heart rate variability, a measure of autonomic activity, in a population of healthy subjects (Henley *et al.,* 2008). Henley *et al.* (2008), propose that manual therapy induces autonomic activity resulting in vasodilatation, smooth muscle relaxation and increased blood flow. It is proposed that these neurophysiological effects may then facilitate an increase in muscle range of motion, decrease in pain perception and/or change in tissue tension.

The aim of this chapter is to systematically review the current empirical evidence for the use of passive manual therapy interventions targeted at the musculoskeletal system as a management approach for COPD patients, focussing on studies which included either performance-based or patient reported measures of pulmonary function.

2.3. Methods

2.3.1. Study design

A systematic review of the published literature on the use of manual therapy techniques in patients with COPD was undertaken.

2.3.2. Study inclusion and exclusion

A scoping search was performed to assist in refining the focus and scope of the review. This involved performing test searches across a number of databases using a range of keywords and a review of other systematic reviews of manual therapy interventions (Hondras *et al.,* 2005; Ernst, 2009). This process facilitated refinement and agreement of the final inclusion and exclusion criteria. Study inclusion and exclusion criteria

Studies were included based on the following criteria:

Participants – Study population included adults with known history of chronic obstructive airways disease, including patients described as having COPD, emphysema and chronic bronchitis. There were no age restrictions.

Interventions – The study population received a form of passive manual therapy, where manual therapy is defined as:

> *'a clinical approach utilizing skilled, specific hands-on techniques, including but not limited to manipulation/mobilisation, used by the physical therapist to diagnose and treat soft tissues and joint structures for the purpose of modulating pain; increasing range of motion; reducing or eliminating soft tissue inflammation; inducing relaxation; improving contractile and non-contractile tissue repair, extensibility, and/or stability; facilitating movement; and improving function' (AAOMPT, 1999; APTA, 2011)*

In order to answer the specific research question studies were excluded where manual therapy interventions were included as part of pulmonary rehabilitation, multimodal programmes or

self-management programmes. Also, studies were excluded where massage techniques or whole interventions were not delivered through hand contact *e.g.* use of mechanical tools/instruments. This is because manual therapy techniques are delivered by professionals (osteopaths, chiropractors, manipulative physiotherapists) trained in the use of the techniques and effectiveness of such techniques is dependent on such expertise.

Comparator – Where there was a comparator, the manual therapy intervention was compared against a control period, a sham technique or alternative manual therapy intervention.

Outcome measures – Studies were included if they measured any lung function parameter. However, the primary outcomes sought were performance-based measures, such as FEV1, FVC and vital capacity. Patient reported measures, such as dyspnoea, were also recorded. Short and long term follow up periods were considered.

Study designs – The ideal study design would have been the randomised controlled trial, as this is considered the gold standard of research design for clinical trials of effectiveness. However a scoping review of the literature suggested limited data available, therefore, quasi-experimental studies, non-randomised controlled trials and before-and-after studies were also included.

2.3.3. Search strategy

Using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Guidelines (PRISMA) and Cochrane collaborative methodology, the following databases were searched: AMED (1979-2010), CINAHL (1979-2010), MEDLINE (1950-2010), Database of Abstracts of Reviews of Effects (DARE), EMBASE (1980-2010), Index to Chiropractic Literature (ICL) (1984-2010), Cochrane Central Register of Controlled Trials (CENTRAL). Search revised January 2012. Citation lists from the included studies were scanned. Studies were also sought from authors

known to have published in this field by exploring relevant internet sites. Included studies were restricted to English language.

The following search terms or MeSH headings were used:

1. Bronchitis, chronic bronchitis, pulmonary disease, chronic obstructive pulmonary disease, chronic obstructive airways disease, chronic airways limitation, COPD, COAD, COLD

2. Mobilisation, mobilization, massage, manipulation (exp), soft tissue manipulation, exercise therapy, muscle stretching, manual therapy

2.3.4. Study Selection

The lead reviewer screened titles and abstracts of studies from the search strategy to exclude irrelevant studies. Full articles were requested where the abstract suggested a relevant study. Where details were missing from the abstract, full articles were requested and screened for eligibility. Eligibility was evaluated by two reviewers, being based on a study satisfying the pre-defined criteria for inclusion. Discrepancies were resolved by discussion.

2.3.5. Data collection and items

Using a standardised form, each reviewer independently extracted the data. Study characteristics included, design, population inclusion/exclusion criteria, manual therapy intervention, professional group, comparator and outcomes measures. Included outcomes were any performance-based or patient reported measures of lung function.

2.3.6. Risk of bias within studies

From the scoping search it was evident that the studies varied with respect to design, intervention, and measures used. A risk of bias appraisal tool was developed. Using Cochrane

Guidelines (Higgins and Green, 2009) and Guidelines for undertaking systematic reviews in healthcare (CRD, 2009) internal validity of individual studies was assessed. The tool combined categories common to studies of differing design such as blinding of assessors, validity of outcome measures with categories unique to different study designs such as randomisation and concealment allocation. Overall, risk of bias was classified for individual studies (low, unclear, high) according to Cochrane Guidelines (Higgins and Green, 2009).

2.3.7. Synthesis of results

It was not appropriate to combine studies for meta-analysis due to the heterogeneity of manual therapy techniques and samples, therefore the results were tabulated for semi-quantitative comparison of study design, population characteristics, intervention, comparator and selected performance-based and patient reported measures of lung function.

2.4. Results

2.4.1. Study selection

From an initial search of databases, 3019 potential studies were identified, with a further 67 studies being identified from searches of grey literature and citation checks. After removal of duplicates, 2957 titles and abstracts of studies were screened for eligibility. 2933 studies were excluded because they did not meet the eligibility criteria, e.g. wrong intervention, or participants, such as pulmonary rehabilitation multimodal programme or asthma. Of the remaining 24 studies, 17 were excluded following review of the full article, mainly because the manual therapy techniques were delivered using mechanical aids or used acupressure. This resulted in seven studies that fulfilled the criteria for eligibility being included in the review. (See Figure 5).

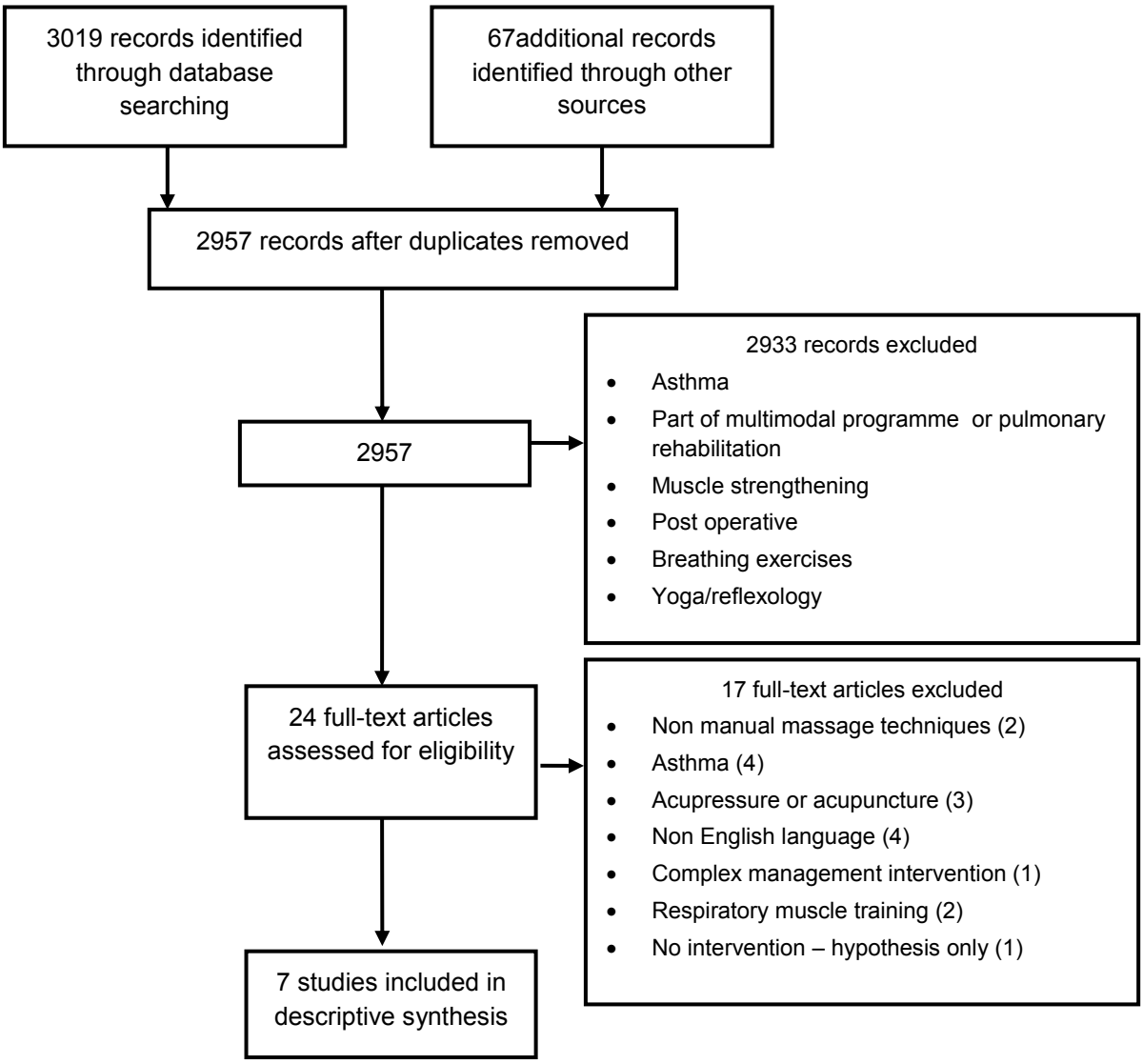


Figure 5. Flow chart indicating identification of studies for the review

All included studies, except one from Australia (Putt *et al.,* 2008), originated from the United States (Howell *et al.,* 1975; Miller *et al.,* 1975; Witt & MacKinnon, 1986; Beekan *et al.,* 1998; Noll *et al.,* 2008, 2009). There were five RCTs (Miller *et al.,* 1975; Witt & MacKinnon, 1986; Noll *et al.,* 2008, 2009; Putt *et al.,* 2008) and two pre-post studies (Howell *et al.,* 1975, Beekan *et al.,* 1998) with three of the RCTs being crossover designs (Witt & MacKinnon, 1986; Noll *et al.,* 2008; Putt

et al., 2008). The sample sizes were generally small, varying between five and 35 participants. The majority of the studies were focused on subjects with evidence of mild to moderate COPD (Miller *et al.,* 1975; Witt & MacKinnon, 1986; Noll *et al.,* 2009; Putt *et al.,* 2008); however, one study used a sample of more severe COPD participants (Noll *et al.,* 2008) was more heterogeneous in nature and also included subjects with asthma (Witt & MacKinnon, 1986). (Table 4)

Table 4. Characteristics of included studies.

Author, Date Country	Title	Design	Population inclusion criteria	Included participants	Intervention & Profession	Comparator	Outcomes (performance based and patient reported measures of pulmonary function)
Miller 1975 USA	Treatment of Visceral Disorders by Manipulative Physiotherapy	RCT	Diagnosis COPD Age; 36-65 years Height; 145-185 cms females 157-190 cms males 41-85kg women, 50-115kg males **Recruitment**; not clear	Treatment n=23 Control n=21 Groups matched for age, sex, and disease severity	**Osteopathic manipulative therapy** aimed at increasing • spinal extension • restrictive movement, • Lymphatic flow by applying pressure to the muscles of thorax through anterior compression of chest. **Plus routine management** **Dose and treatment duration** 2 x per week (duration not given)	**Routine management** only; including as necessary chemical, medical, adjunctive therapy inc. bronchodilators, aerosol, IPPB, breathing exercises, postural drainage, graded exercises, supplementary oxygen.	**FEV_1, FEV_2, FEFR, VC, FRC, RV, TLC** **PO_2, PCO_2** **Questionnaire on Respiratory Symptoms** Musculoskeletal exam- included hypermobility, costovertebral dysfunction, side flexion or rotation changes, skin drag, AP or lat curvature of spine, muscle tension pH Carbon monoxide diffusion studies MVV Minute ventilation measured Tidal volume **Reassessment**; length of follow-up not given

Author, Date **Country**	**Title**	**Design**	**Population inclusion criteria**	**Included participants**	**Intervention & Profession**	**Comparator**	**Outcomes** **(performance based and patient reported measures of pulmonary function)**
Howell, Allen, Kappler 1975 USA	The influence of osteopathic manipulative therapy in the management of patients with chronic obstructive lung disease	Pre-post study	Objective evidence of COPD according to ATS criteria **Recruitment**; not clear	N= 17 11/17 studied for minimum 9 months	**Osteopathic manipulative therapy** directed at mobilising specific spinal segment where intervertebral stiffness was detected or paravertebral tissues were abnormal. **Plus routine management**; attention to bronchial hygiene, pharmacology as required and education. **Dose and treatment duration** Frequency and dose not explicit; suggestive of intermittent throughout duration of study	None	**FEV_1, FVC, FEF $_{25-75\%}$, FEF $_{200-1200}$** **%VC, %RV, %TLC (VC-FVC/VCx100)** **PO_2, O_2 sat, PCO_2.** **Composite severity score** **Reassessment**; at follow-up 1month, and 3 months after commence of treatment. Then 3 month intervals thereafter for a total of a year.
Witt & MacKinnon 1986 USA	Trager Psychophysical Integration (TPI); A method to improve chest mobility of patients with chronic lung disease	Cross over RCT	Any documented chronic lung disease. **Recruitment from** Wake County Lung Association Respiratory Health Club	N=12 (4 male) Mean age 64 years 2 had asthma only;	**Trager Psychophysical Integration** (TPI) delivered by same **physical therapist** trained in TPI TPI – the use of gentle painless, passive movements. Intervention customised to patient but set treatment protocol with	No intervention for 2 week period	**FVC, FEV_1/FVC, FEV_3/FVC** **Breathing difficulty – 10-pt Likert scale** Chest expansion Heart rate Respiratory rate

Author, Date Country	Title	Design	Population inclusion criteria	Included participants	Intervention & Profession	Comparator	Outcomes (performance based and patient reported measures of pulmonary function)
				7 had emphysema only, 3 emphysema + asthma or bronchitis.	anticipated progression. Goals for all subjects • To increase mobility of neck, chest and abdomen • to provide kinaesthetic awareness of being able to move body part freely **Dose and treatment duration** 4 x 20-minute sessions, 2 week duration		Patient opinion **Reassessment**; following end of each 2-week test period (control and intervention phase) with further follow up 2 weeks after end of second test period
Beeken, Parks, Cory, Montopoli 1998 USA	The Effectiveness of Neuromuscular Release Massage in Five Individuals with COPD	Pre-post study	Moderate chronic obstructive lung disease >1 litre FEV_1 and 40% predicted FEV_1 and/or FVC **Recruitment**; self referral (n=2),	N=5 (4 male) Age 57-74 yrs Mixed presentation COPD, emphysema, interstitial lung disease	**Neuromuscular Release Massage Therapy (NMRT) by Certified massage therapist.** **NRMT** aims to relieve pain and restore function in presence of chronic muscle spasm. It is described as: • Application of pressure and	None	**FEV_1, FVC, FEV_1/FVC** **Borg dyspnoea scale (VAS)** **O_2 saturation** Peak flow Thoracic gas volume Breath hold time Self-reported daily

Author, Date Country	Title	Design	Population inclusion criteria	Included participants	Intervention & Profession	Comparator	Outcomes (performance based and patient reported measures of pulmonary function)
			physician referral (n=3)		resistance to muscles to promote healing. • Pressure is applied to trigger points to increase local blood flow, facilitate lymphatic drainage and elicit muscle relaxation. • Diaphragmatic release – trigger point application during exhalation **Dose and treatment duration** 1 x 1-hour treatments at same time and day each week. 24 weeks duration		activities **Reassessment**; at 24 week follow up
Noll, Degenhardt, Johnson, Burt 2008	Immediate Effects of Osteopathic Manipulative Treatment (OMT) in Elderly Patients with COPD	Double blind RCT Stratified by COPD	Known history of COPD or from spirometry screening Aged 65+ yrs with	N=35 (18 male) OMT n=19 Sham n =17	7 standardised **Osteopathic Manipulative Techniques** (Soft Tissue Massage, Rib raising, indirect Myofascial Release, sub occipital	Sham subjects received same structural examination but no treatment of specific dysfunctions.	**FVC, FEV_1, FEV_1/FVC**, **Subjective report of effect on breathing** 21 pulmonary

Author, Date Country	Title	Design	Population inclusion criteria	Included participants	Intervention & Profession	Comparator	Outcomes (performance based and patient reported measures of pulmonary function)
USA		severity	$FEV_1/FVC<70\%$ **Recruitment**; from outpatient office setting	Mean age: OMT-69.6yrs Sham-72.2yrs Mean $FEV_1/FVC\%$ = 46% both groups	decompression, Thoracic inlet Myofascial release, pectoral traction, Thoracic lymphatic Pump with activation. **Plus**, subjects received structural examination and treatment of specific somatic dysfunction using indirect Myofascial release, high velocity, low amplitude thrust techniques or muscle energy techniques. **Dose and treatment duration** 20 minutes treatment One session	Sham treatment in supine lying using light touch applied to same anatomical regions as in OMT group, rib cage, light palpation of paraspinal muscles and thoracic spine as well as rib motion detection and light 'clopping' in side lying to reflect OMT techniques in intervention group. 20 minutes treatment One session	function parameters in total Spirometry and plethysmography Trained respiratory therapist **Reassessment**; 30 minutes post treatment.
Putt, Watson, Seale and Paratz	Muscle stretching techniques increases vital capacity and range of motion in	Double blind crossover RCT	COPD $FEV_1/FVC<70\%$	N= 14 Mean age 66.4yrs	**Proprioceptive Neuromuscular Facilitation technique by Physiotherapist** in position of 90-degrees horizontal abduction at	Sham technique: passive movement of flexion and extension in 25-degrees abduction. Repeated 3 times	**VC, Perceived Dyspnoea (Borg),** Axilla chest expansion, Xiphisternum chest

Author, Date Country	Title	Design	Population inclusion criteria	Included participants	Intervention & Profession	Comparator	Outcomes (performance based and patient reported measures of pulmonary function)
2008 Australia	patients with COPD		**Recruitment from** completion of 7 week Pulmonary Rehab programme in hospital setting	Mixed presentation COPD, chronic asthma	shoulder and 90-degrees elbow flexion. 6-second isometric contraction of pectoralis major muscle, followed by relaxed and passive stretch in opposite direction. **Dose and treatment duration** 2 treatments on 2 consecutive days Washout period; 3 days	through resistance free range of motion. Isometric biceps contraction in mid abduction for 6-seconds. Each intervention performed 6 times each arm, with 30-second rest between each. 2 treatments on 2 consecutive days	expansion, respiratory rate, right and left shoulder horizontal extension goniometer **Reassessment**; after each session
Noll, Johnson, Baer, Snider 2009 USA	The immediate effect of individual manipulation techniques on pulmonary function measures in persons with COPD	Crossover RCT	Aged 50+ yrs with a history of COPD FEV_1/FVC <70% of the predicted value **Recruitment from**	N=25 (14 male) Mean age 68yrs	**Osteopathic manipulative techniques** were used. Treatments: -Thoracic Lymphatic Pump without activation; pressures applied in the pectoral region during exhalation and some resistance	Minimal touch served as a control.	**FVC, FEV_1, FEV_1/FVC**, **Subjective report of effect on breathing and perception of health side effects** FEF 25-75%, FEF max, MVV, SVC, IC, ERV, TGV, RV, TLC, RV/TLC, Airways

Author, Date Country	Title	Design	Population inclusion criteria	Included participants	Intervention & Profession	Comparator	Outcomes (performance based and patient reported measures of pulmonary function)
			a variety of sources.		offered during inhalation to induce respiratory muscle activation. -Thoracic Lymphatic Pump with activation; pressures applied in the pectoral region during exhalation and brisk removal of hands during inhalation to induce a negative pressure in the thorax. -Myofascial release where restriction or asymmetry noted; diaphragm, thoracic inlet, rib cage, cervical region. -Rib raising; anterior-posterior mobilisation of ribs in supine lying **Dose and treatment duration** A single session for each intervention, lasting 5 minutes to 10 minutes		resistance. Spirometry and plethysmography Trained respiratory therapist **Reassessment**; 30 minutes post treatment

Author, Date Country	Title	Design	Population inclusion criteria	Included participants	Intervention & Profession	Comparator	Outcomes (performance based and patient reported measures of pulmonary function)
					for MRT. Order randomised. Washout period; 4 weeks		

COPD; chronic obstructive pulmonary disease, FEF; forced expiratory function, FEV_1; forced expiratory volume in one second, FEFR; forced expiratory flow, FRC; functional residual capacity, RV; residual volume, TLC; total lung capacity PO2; partial pressure of O2, PCO2; partial pressure of CO2 VAS; visual analogue scale, MRT; Myofascial release technique, MVV; maximum voluntary ventilation, SVC; slow vital capacity, IC; inspiratory capacity, ERV; expiratory reserve volume, TGV; Thoracic Gas Volume, VC; vital capacity,

The studies included four passive interventions, which used a range of osteopathic spinal manipulative techniques given by an osteopath (Howell *et al.,* 1975; Miller *et al.,* 1975; Noll *et al.,* 2008, 2009), one using massage from a certified massage therapist (Beekan *et al.,* 1998), one muscle stretching by a physiotherapist (Putt *et al.,* 2008) and one using passive movements given by a physical therapist aimed at increasing neck, chest and abdominal mobility (Witt & MacKinnon, 1986). Doses with respect to length of treatment in time and frequency of interventions were variable. The treatment duration across the studies extended from a single session (Noll *et al.,* 2008, 2009) to many sessions over a prolonged period, with the longest intervention being performed over a nine month period (Howell *et al.,* 1975). The comparators within the RCTs included one of the following: routine management, light touch, a technique that the researchers deemed non therapeutic, or no intervention.

With the exception of one study (Putt *et al.,* 2008) that only measured vital capacity as a means of assessing pulmonary function, the other six included as a minimum, FEV_1 and FVC (Howell *et al.,* 1975; Miller *et al.,* 1975; Witt & MacKinnon, 1986; Noll *et al.,* 2008, 2009). Four of these studies included multiple measures of pulmonary function, with one study reporting on 21 parameters of pulmonary function (Noll *et al.,* 2008). Five out of the seven studies only considered immediate effects (Howell *et al.,* 1975; Miller *et al.,* 1975; Witt & MacKinnon, 1986; Noll *et al.,* 2008, 2009) and did not follow up results beyond a next day telephone evaluation (Noll *et al.*, 2008, 2009). Patient reported measures were reported in 6 of the studies (Miller *et al.,* 1975; Witt & MacKinnon, 1986; Beekan *et al.,* 1998; Noll *et al.,* 2008, Putt *et al.,* 2008; Noll *et al.,* 2009), but principally focused on specific questions on side effects, breathing difficulty, activity levels, sleeping, etc., rather than using validated patient reported measures. Of the two studies that used the Borg dyspnoea scale to measure dyspnoea (Beekan *et al.,* 1998; Putt *et al.,* 2008), only one reported the results (Putt *et al.,* 2008).

2.4.3. Study quality and risk of bias

Both the reporting and conduct of the studies was generally very poor (Table 5). Six studies were classified as having a high risk of bias (Howell *et al.,* 1975; Miller *et al.,* 1975; Witt & MacKinnon, 1986; Noll *et al.,* 2008; Putt *et al.,* 2008), with only the most recent trial being rated as having low risk (Noll *et al.,* 2009). Studies were small and contained heterogeneous populations with little structure to recruitment. Although five described themselves as RCTs (Miller *et al.,* 1975; Witt & MacKinnon, 1986; Noll *et al.,* 2008, 2009; Putt *et al.,* 2008), three failed to report the statistical tests used or conduct the correct statistical tests to compare intervention with control (Miller *et al.,* 1975; Witt & MacKinnon, 1986; Putt *et al.,* 2008), and one was subject to the problems of multiple testing (Noll *et al.,* 2008). Intention to treat analysis should have been performed to account for attrition or missing data. In two of the five RCTs, randomisation methods were unclear (Witt & MacKinnon, 1986; Noll *et al.,* 2008) and only the most recent study (Noll *et al.,* 2009) described adequate allocation concealment. It is recognised that blinding of participants would be difficult; however, in four of the studies, outcome assessors were blinded (Miller *et al.,* 1975; Beekan, 1998; Noll *et al.,* 2008; 2009). Valid performance-based measures of pulmonary function were used in the majority of studies, although patient reported measures were generally inadequate focused on broad subjective questions of well being rather than validated questionnaires relating to quality of life or perceived dyspnoea; St Georges Respiratory Questionnaire or the Medical Research Council (MRC) Dyspnoea Scale being examples of tools that could be utilised. Furthermore, the follow-up period in most studies was restricted to immediate effects.

Table 5. Risk of Bias Assessment

Sources of bias accounted for and other quality issues	Miller 1975	Howell, Allen *et al.,* 1975	Witt & McKinnon 1986	Beekan *et al.,* 1998	Noll *et al.,* 2008	Putt *et al.,* 2008	Noll *et al.,* 2009
Clearly defined research question	√	√	√	√	√	√	√
Power calculation/sample size	N=23	N=17	N=12	N=5	N=35	√ N=14	√ N=25
Control group or period included	√ RCT	No; pre/post	√ Cross-over RCT	No; pre/post	√ RCT	√ Cross-over RCT	√ Cross-over RCT
Washout period sufficient to avoid carryover effect	n/a	n/a	n/a due to study design	n/a	n/a	Probably not; only 3 days	√
Recruitment strategy/sample representative of COPD	Recruitment / diagnostic criteria not clear	Recruitment not clear	Recruited from lung association; mixed presentation	2 self-referrals and 3 from local physician.	√ COPD outpatient	√	√ COPD outpatient & adverts
Randomization – was this performed and adequately described	√ Random number tables + matched pairs	n/a	Not clear how they were randomised	n/a	Not clear how they were randomized	Computer-generated random numbers	√ Blocked and balanced
Was the allocation adequately concealed?	Not clear	n/a	Not clear	n/a	Not clear	Not clear	√
Were the groups comparable at baseline	Only lung function parameters given	n/a	Yes – cross-over	n/a	Small numbers therefore balance not achieved in all parameters	√ Cross-over	√ Cross-over
Blinding of participants and study personnel to intervention	√ NMS examination blinded	n/a	No	No	√ Outcome assessors blinded	√ Participants and assessors blinded	√ Outcome assessors blinded
Performances based measures of– validity & reliability considered (spirometry)	No	Disease severity score – no apparent validation	√	√	√	√	√
Patient reported outcomes– validity considered & reliability(questionnaires on subjective well-being)	No	n/a	No	Not clear	Not validated	Not clear	√

Evidence of outcome measures performed, but not reported	√	No	√	√ Borg scale not reported	No	No	No
Statistical tests appropriate	No statistical tests	Not clear	Analysis appeared to focus on pre/post-test changes	Paired differences t-test?	√ But multiple testing.	Analysis appeared to focus on pre/post-test changes	√
Missing data accounted for	No – 44 cases but only data on 23 provided	Data only analysed on 11/17; no reasons given	√	No	Yes	Data only analysed on 10/14; no reasons given	√
Follow up period of sufficient length	Unclear	Probably – 9mths	Follow-up short – only 2 weeks.	Probably – 24 weeks	No – immediate effects only	No – immediate effects only	No – immediate effects only
Risk of bias	**High**	**High**	**High**	**High**	**High**	**High**	**Low**

2.4.4. Summary of study results

Table 6 gives an overview of the main results with an indication of the design, intervention and study quality for context. Few studies showed any meaningful results; the poor quality precluded any detailed conclusions to be drawn. Across a range of lung function measures, there was no consistency in the either the direction or magnitude of change after intervention. Lack of correct analysis meant that, in several studies, the intervention was not statistically compared against the control group. Despite possible mild side effects initially, when questioned later, patients often reported feeling better after the intervention (Miller *et al.,* 1975; Beekan *et al.,* 1998; Noll *et al.,* 2008; 2009), although this was also noted for the controls in some studies (Noll *et al.,* 2008; 2009). Overall, all studies lacked adequate length of follow-up with valid patient reported and performance-based outcome measures.

Table 6. Summary of study results

	Design & intervention	Results	Comments/study quality
Miller 1975	RCT 2 x per week **osteopathic manipulative therapy** aimed at increasing spinal extension, lymphatic flow compared to routine management N=23	<u>Performance based measures of pulmonary function</u> <u>FEV_1</u> OMT: increased 2.1L (2.9%) Control: reduced 2.4L (3.8%) <u>VC</u> OMT: increased 0.5L (13%) Control: increased 0.1L (4%) p>0.05 <u>TLC</u> OMT: increased 1.0L (24%) Control: increased 0.1L (2%) <u>O_2 sat</u> OMT: reduced 3.6 (3.8%), Control: reduced 3.3 (3.8%) <u>Patient reported measures</u> 92% stated positive effects for OMT (less colds, URTI, less dyspnoea)	○ Sample small & recruitment strategy unclear ○ Methodology unclear ○ & not reproducible. No *a priori* power calculation ○ Statistical tests not included. MCID not given ○ Missing data unaccounted for ○ Follow up period unclear
Howell, Allen *et al.,* 1975	Pre/post case series **Osteopathic manipulative therapy** as part of management that included: attention to bronchial hygiene, pharmacology as required and education. 9 month f/u N=11	<u>Performance based measures of pulmonary function</u> *(Composite severity score reduced over time* *10.7% improvement in severity score overall)* Significant improvement in 4 parameters (p< 0.05) including TLC: 2% increase O_2 sat: 1% increase <u>Patient reported measures</u> N/A	○ Sample small & recruitment strategy unclear ○ No control ○ No *a priori* power calculation ○ Dose and treatment duration unclear ○ No details of statistical tests given. ○ Missing data unaccounted for
Witt & McKinnon 1986	Crossover RCT 4 x 20-min sessions of **TPI** (2 x/week for 2 weeks) or control (no treatment)	<u>Performance based measures of pulmonary function</u> *(Data pooled for pre/post analysis)* FVC increased by 0.24L (13.02%)(p<0.05) FEV_1/FVC reduced by 6.74% FEV_3/FVC reduced by 0.34 %	○ Sample very small and heterogeneous ○ Design unclear. No *a priori* power calculation ○ No blinding ○ Results very unclear re statistical tests, including data pooling and analysis pre and post changes and

	Design & intervention	Results	Comments/study quality
	N=12	FVC % predicted increased by 5.4% <u>Patient reported measures</u> Self reported subjective increase in sleep, energy	missing data on patient reported outcomes
Beekan *et al.,* 1998	Pre/post case series **Massage therapy** directed at diaphragm. 24 x 1-hr weekly treatments. N=5	<u>Performance based measures of pulmonary function</u> *(Pre/post analysis)* FVC decreased by 0.01L (0.3%) FEV_1 decreased by 0.09L (6%) O_2 saturation↑~1% <u>Patient reported measures</u> QOL not reported Perception dyspnoea not reported	○ Very sample small and heterogeneous ○ Design; no control, no *a priori* power calculation ○ No blinding ○ Methods unclear ○ Results very unclear re t-tests, analysis pre and post changes and missing data on patient reported outcomes
Noll *et al.,* 2008	Double blind RCT Sham (20 mins) or 7 specified **OMT** techniques (STM, Rib , MRT, Cranial , soft tissue stretching lymph pump and other indicated techniques (20 mins) Additional techniques given where deemed appropriate by therapists in OMT group- MRT, MET, HVLAT N=35	<u>Performance based measures of pulmonary function</u> Statistically significant difference between study groups for 8 of the 21 pulmonary function parameters. A tendency for reduced expiratory volume, increased lung volume and reduced airways resistance. Comparison of change within groups and significance of difference FEV_1 (L) - OMT decreased by 0.04 (3%) - Sham increased by 0.2 (2%) where p= 0.06 FVC (L) - OMT decreased by 0.14 (6%) - Sham decreased by 0.05 (2%) - where p= 0.14 FEV_1/FVC (%) - OMT increased by 1.15 - Sham decreased by 0.53 where p= 0.83 TLC (L)	○ Sample small, severe COPD and elderly ○ Design; unclear re randomisation Inclusion of 21 measures of pulmonary function. No *a priori* power calculation ○ Results; Multiple testing of parameters, immediate effects only. MCID not given

	Design & intervention	Results	Comments/study quality
		- OMT decreased by 0.5 - Sham decreased 0.28 (p=0.02) <u>Patient reported measures</u> Health benefit; most subjects (both groups) felt benefit from manual therapy Breathing; most subjects (both groups) reported subjective improvement	
Putt *et al.,* 2008	Double blind crossover PNF hold/relax stretching technique for shoulder over 2 days vs. sham 2 days – passive movement and isometric biceps Washout period 3 days N=10	<u>Performance based measures of pulmonary function</u> *(Pre/post analysis)* Post intervention VC increased by 0.2L (9.6% increase) Post sham VC reduced by 0.2L (5%) (p=0.005) <u>Patient reported measures</u> Perceived dyspnoea; no difference between groups (p=0.41) or over time (p=0.35)	○ Sample small and heterogeneous ○ Methodology; no *a priori* power calculation ○ Intervention, single muscle intervention ○ Results; no FEV_1/FVC ○ Attrition with 4 drop outs ○ No intention to treat analysis ○ Focused on pre and post changes rather than comparison between intervention ○ Immediate effects only
Noll *et al.,* 2009	Cross over RCT 5 single sessions of each technique random order Washout period 4 week between each technique Minimal touch, TLP with & without activation Myofascial release Rib raising N=25	<u>Performance based measures of pulmonary function</u> Paper details pre/post results for each technique. Possible mild worsening but each technique had different effects on pulmonary function. Overall there was no significant difference between techniques or % change from baseline. <u>Patient reported measures</u> <u>Improved health</u> Minimal touch control 41% TLP with Activation 76% TLP without Activation 67% Rib raising 68% Myofascial release 53% <u>Improved breathing</u> Minimal touch control 44% TLP with Activation 74%	○ Sample small and heterogeneous ○ No *a priori* power calculation ○ Results; Immediate effects only. MCID not given ○ Single session of each intervention and with 4-week washout total treatment duration 20-weeks.

	Design & intervention	Results	Comments/study quality
		TLP without Activation 57% Rib raising 79% Myofascial release 50% <u>Other measures</u> Side effect; general mild discomfort 6%-19%	

FEV; Forced expiratory volume; FEV_1; Forced expiratory volume in 1 second FVC; forced vital capacity, HVLAT; high velocity low amplitude thrust, O_2sat; oxygen saturation, OMT; Osteopathic manipulative therapy, MCID; Minimal clinical importance difference, MET; muscle energy technique, MRT; Myofascial release technique, PNF; proprioceptive neuromuscular facilitation, QOL; quality of life, STM; soft tissue massage, TLC; total lung capacity, TLP; thoracic lymph pump, TPI; Trager Psychophysical Integration, URTI; upper respiratory tract infection, VC; vital capacity,

The only study to achieve adequate quality (Noll *et al.,* 2009), was a cross-over RCT comparing four single sessions of different osteopathic manipulative techniques with a "minimal touch" control session in 25 COPD patients recruited from a variety of sources. Physiological measures of pulmonary function (FEV_1, FVC) overall changed minimally (<1.5%) following OMT and each intervention failed to achieve statistical significance compared to the control intervention. Patient self-reported measures did improve following osteopathic manipulative techniques for rating of ´improved health´ (53-76% for the different techniques used) compared to the control (41%), and ´breathing difficulty´ (50-79% for the different techniques used) compared to the control (44%). Statistical analysis of these results was not performed. The main problem with this study was lack of follow-up beyond the immediate post-intervention 30 minute period, and validated patient reported measures. Overall, evidence supporting the use of manual therapy in the management of COPD is lacking.

The results of this review highlight the lack of good quality, well-designed, controlled clinical trials, where evaluation of interventions extends beyond immediate effects and utilises validated performance-based and patient reported measures of pulmonary function.

2.5. Discussion

This systematic review is the first to evaluate the evidence for the effects of passive manual therapy interventions on pulmonary function in subjects with COPD. Overall, from the seven studies identified, there is little evidence to currently support or refute the use of manual therapy interventions in the management of COPD. Key problems were poor methodological quality of both reporting and conduct of studies; heterogeneity of study type, population, interventions and outcomes; inadequate statistical analysis and inadequate length of follow-up. This compares with recent reviews in asthma, which report that there is insufficient evidence to support or refute use of manipulative therapy for people with asthma (Hondras *et al.,* 2005; Ernst, 2009).

2.5.1. Variability of interventions

Within the scope of passive manual therapy, there is a plethora of techniques to choose from, and all techniques are both patient and therapist dependant. The approaches used in the included studies varied considerably from spinal manipulative therapy to massage to muscle stretching. Whilst all of these are manual therapy approaches, the proposed therapeutic and physiological effects of each differ. The theoretical or empirical evidence supporting the use of the chosen techniques in the included studies was unclear, with most justifying their aim from anecdotal evidence or the theoretical basis that enhanced joint and muscle flexibility in the thoracic region could improve lung function and reduce the work of breathing.

The doses and frequency of the included interventions varied considerably, from a single session to several sessions over a period of time as part of a course of treatment, where the latter is

more reflective of clinical practice. The interventions themselves also varied from a single technique to a number of techniques forming an intervention. Again, the latter of these better reflects current UK clinical practice, yet is more difficult to standardise for the purpose of research.

The therapists carrying out the interventions included a number of professional groups who perform manual therapy techniques, osteopaths, chiropractors, a massage therapist and physiotherapists. Whilst all utilise manual therapy, each group have different preferences, notwithstanding levels of expertise. Manual therapy, as an approach, is difficult to standardise, and the application of techniques is fundamentally patient specific, dependant on the length, strength, mobility, stiffness, etc. of the target tissues. Furthermore, the applied pressures and forces used are determined by the therapist based on a subjective assessment of 'tissue dysfunction'.

2.5.2. Outcome measures

The studies included used a range of outcome measures, with the main emphasis being on performance-based measures of pulmonary function using spirometry rather than patient reported measures of change. All but one study used measures of FEV_1 and FVC as primary measures of pulmonary function, with two studies including an exhaustive list of 21 separate measures of pulmonary function. Whilst descriptive changes in lung function were provided in all studies, the minimum clinically important differences for each outcome measure were not reported for any of the included studies. The published minimum clinical important difference for FEV_1 of 200mL plus 12% above baseline values (Gross, 2005) was achieved in two studies (Miller *et al.,* 1975; Putt *et al.,* 2008). However risk of bias was rated high, raising doubt about the meaningfulness of the results. The patient reported measures were limited to Borg perceived breathing difficulty scale or a subjective report on breathing. The effect of the intervention on daily activities was reported in two studies with a one day telephone follow up

(Noll *et al.,* 2008; 2009). The outcomes were generally measured immediately post intervention, with telephone follow up for side effects after one day and effect on daily function (Noll *et al.,* 2008; 2009). For patients with chronic lung disease, the very nature of the interventions can be tiring, induce treatment soreness of musculoskeletal structures and, could themselves adversely affect a patient's effort/ability to perform the pulmonary function tests. This could, in turn, underestimate the potential benefits of manual therapy. In two of the included studies the interventions resulted in an immediate slight worsening in pulmonary function (FEV_1, FVC) (Noll *et al.,* 2008; 2009). This could be as a result of manual therapy-induced bronchospasm and/or loosening of airways secretions, which could exacerbate air trapping and affect post intervention measures of pulmonary function (Noll *et al.,* 2009). However empirical evidence to support this is currently lacking. Paradoxically, Noll *et al.* (2008; 2009) report beneficial effects on subjects' self-reported wellbeing post intervention. This could be a result of the possible influence of placebo or manual therapy induced endogenous opioid release (Noll *et al.,* 2009).

Future studies should consider greater use of validated patient reported measures, such as the St George's Respiratory Questionnaire (SGRQ) or COPD Self Efficacy Scale, over a longer term follow up period, which may better reflect the effect of the intervention on patient reported measures of function, rather than primarily relying on performance-based measures of lung function, such as spirometry. Only one study included a measure of thoracic mobility, measuring change in chest expansion at the axillary and xiphisternal levels pre- and post-intervention, and found no difference with their intervention (Putt *et al.,* 2008). Inclusion of a performance based musculoskeletal outcome measure would be useful in future studies to evaluate a possible underlying biomechanical effect. Additionally, in light of the work by Bentsen *et al.* (2011), further research is required to better understand the prevalence, aetiology and severity of pain across the different stages of the disease, using validated pain questionnaires.

2.5.3. Methods

The samples, recruitment strategies and research settings used in these studies were all unclear. Evidence of competence and adherence to American Thoracic Society Guidelines for the pulmonary function tests was given in just three studies (Noll *et al.,* 2008; 2009; Putt *et al.,* 2008), raising questions about the reliability and validity of the pulmonary function measures. Expertise in manual therapy for the intervention was not included in any studies; hence raising doubt as to any attempts to standardise the intervention given. Blinding in the use of manual therapy interventions is very difficult to achieve, although double blinding was achieved in two of the included studies (Putt *et al.,* 2008; Noll *et al.,* 2009). In many of the studies, the assessors were blinded to treatment allocation. Future studies should also consider methodologies to enable participant blinding to further reduce the risk of bias. Randomisation was frequently not preserved, and the statistical analysis limited to simply pre/post comparisons.

2.5.4. Limitations of the review

The review was conducted to published standards, although one limitation was the possibility of publication bias, due to exclusion of non-English language articles.

2.6. Summary

From this review there is little evidence to support or refute the use of passive manual therapy techniques in clinical practice to improve lung function in COPD patients. There is also little evidence to support the inception of a larger, better designed RCT given the diversity of techniques available, lack of understanding of the relationship between form and function in the thoracic region and its relationship with pulmonary function. At this stage, further exploratory research is required to describe the nature and extent of changes in the musculoskeletal system, and whether any changes that do exist exhibit a meaningful relationship with performance-based and patient reported measures of pulmonary function. Interestingly, this has been done in other respiratory diseases. A recent study by Lunardi *et al.* (2010) compared musculoskeletal

changes in subjects with asthma of varying degrees of severity (n=30) to a matched control group (n=15). They concluded that disease-induced changes do occur in postural alignment, muscle length and pain of musculoskeletal origin ($p<0.05$ for ten measures of posture, cirtometry at axillary and xiphoid level; forward head and shoulder posture; shoulder elevation and internal rotation; muscle shortening with Schober, finger-to-floor and Stibor tests). Whilst the extent of changes did not appear to relate to disease severity, a relationship between some of the musculoskeletal changes appeared to relate to age of onset. Participants who had had asthma since childhood (up to 12 year of age, n=13) were compared to those who had onset after 12 years of age n=17 with statistically significant difference being noted for xiphoid expansibility ($p=0.05$) and shoulder internal rotation ($p=0.02$). These findings are not altogether surprising, given many individuals experience asthma from childhood prior to musculoskeletal maturity and, therefore, could be considered more susceptible to extrinsic influences on musculoskeletal development, such as accessory muscle activity leading to protracted shoulders and poking chin. Whilst Lunardi *et al.* (2010) did evaluate posture and chest wall mobility using a tape measure to determine the difference between the chest circumference at maximal inspiration and maximal expiration at the axillary and xiphoid levels, no measures of thoracic mobility were included, possibly due to the limited motion analysis research in the thoracic region as a whole.

Chapter 3. MOTION ANALYSIS AND SOFT TISSUE ARTEFACT IN THE THORACIC SPINE

Publication

Heneghan NR, Balanos GM. (2010). Soft tissue artefact in the thoracic spine during axial rotation and arm elevation using ultrasound imaging: a descriptive study. Manual Therapy 15(6):599-602. (Appendix 5)

3.1. Abstract

Purpose: The aim of this chapter is to provide a review of motion analysis systems used in the thoracic spine and subsequently evaluate soft tissue artefact, during thoracic axial rotation.

Relevance: Much of the current understanding of thoracic motion analysis is based on the use of skin sensors or markers. Soft tissue artefact, movement occurring between the skin and underlying bone, is readily acknowledged by researchers as a source of measurement error, yet to date has not been quantified.

Methods: Using ultrasound imaging of three thoracic vertebrae (T1, T6, T12), this study reports the extent of soft tissue artefact in the thoracic spine during axial rotation in sitting using 30 asymptomatic individuals. Additionally range of motion was measured using the Polhemus, Liberty™ motion analysis system. Range of motion was measured using a motion sensor attached to the ultrasound transducer, thus giving confidence that motion was a product of vertebral motion and not just movement of the overlying skin.

Results: The findings from this study indicate that soft tissue artefact in the mid-thoracic region (T6) ranged between 14-16 mm for 35-degrees of rotation. Skin tissue artefact at the levels of T1 and T12 were considerably less, ~15mm for 75-degrees rotation, 10 mm for 13-degrees respectively.

Conclusion: The results of this study suggest that soft tissue artefact is a considerable and variable source of error in all regions of the thoracic spine, but most notably for the mid-thoracic region during axial rotation rendering existing measurement approaches unsuitable for accurate measure of axial rotation.

The aim of this chapter is to:

1. Briefly review anatomy and mobility in the thoracic region

2. Critically review motion analyses methods in the thoracic region

3. Report findings from a study that quantified soft tissue artefact in 3 regions of the spine during thoracic axial rotation.

3.2. Introduction

The thoracic spine compared with the cervical and lumbar regions is relatively immobile (Figure 6), designed to provide support and structural protection to vital internal organs, such as lungs and heart. As well as the bony configuration describe in chapter 1 contributing to the stiffness of the thoracic cage, it is of note that the thoracic intervertebral discs are relatively thinner than in other spinal regions, with a disc to vertebral body height ratio of 1:5, compared to 2:5 and 1:3 for the cervical and lumbar spine respectively (Edmondston & Singer, 1997). This complex biomechanical design affords little flexibility (passive and active) in the sagittal and frontal planes, with the largest range of motion being that of axial rotation around a vertical axis, also named the 'Y-axes' by Panjabi & White (1990) (see Figure 7). From research using cadaveric models, ranges of motion for all spinal regions and planes of motion have been reported, illustrating the relative motion in each spinal region (Lee, 1993). It should be noted that actual ranges of motion may, in fact, be less than those documented here, as use of cadavers without chest wall intact may further limit available range. This model does not specifically include the rib, although from the evidence informed description of anatomy and biomechanics provide in chapter 1, it is accepted that rotation around the 'Y-axes' is coupled with anterior rotation of the contralateral rib and posterior rotation of the ipsilateral rib (Lee, 1993).

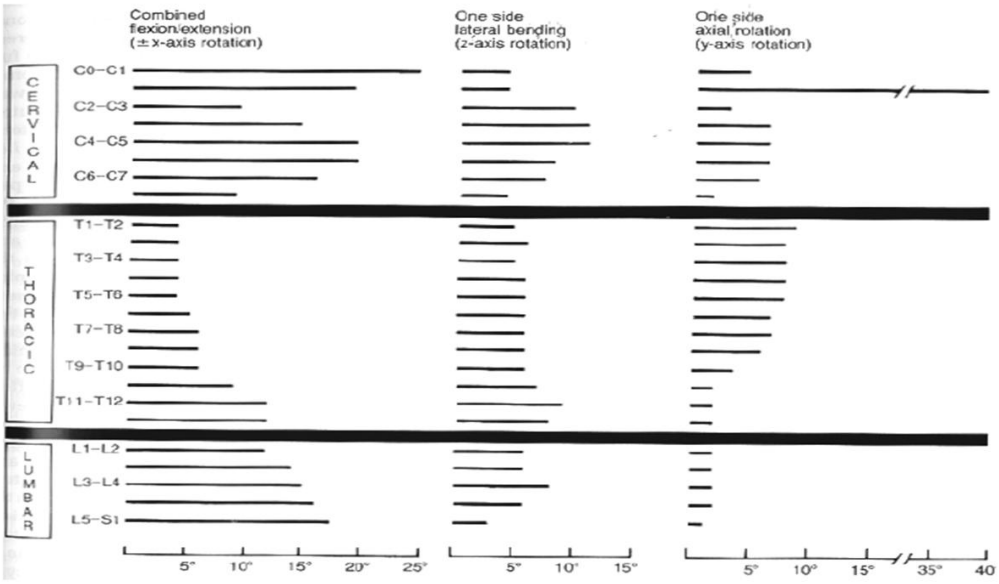


Figure 6. Ranges of motion throughout the normal spine. From White & Panjabi *Clinical Biomechanics of the Spine.*

Figure 6. Ranges of motion in the spinal regions (Panjabi & White, 1990)

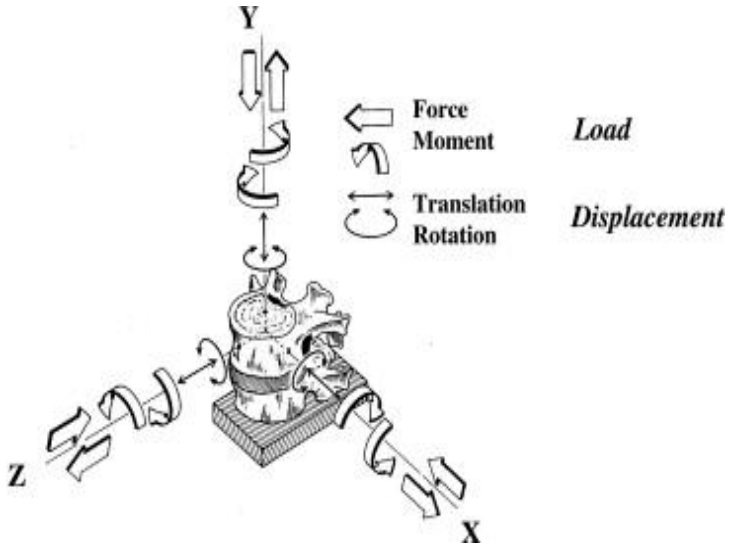


Figure 7. Panjabi orthogonal model (Lee, 1993)

3.3. Measurement of thoracic spine motion

The ability to evaluate active range of motion is fundamental to clinical practice and research into spinal disease and dysfunction. Ethical issues associated with radiation exposure and high

costs prohibit the widespread use of x-ray, considered the gold standard for motion analysis in the spine (Willems *et al.,* 1996). For that reason, other tools have been developed to measure spinal range of motion. A wealth of studies exploring tools for motion analysis within the cervical and lumbar regions have been published (Mannion & Troke, 1999; Jordon, 2000). However, it is only recently that consideration has been given to the evaluation of movement occurring in the thoracic region. Research in the cervical and lumbar spine regions has been driven by high costs associated with whiplash associated disorder and occupational low back pain respectively. Until recently, much of our understanding of thoracic spine motion and biomechanics was based on mathematical models (Andriacchi *et al.,* 1974; Saumarez, 1986), theoretical models (Lee, 1993) or *in vitro* studies (Panjabi *et al.,* 1990).

Due to limitations of modelling and *in vitro* studies and with rapid technological advances, studies have evolved to include *in vivo* measurement tools to evaluate static position and dynamic active motion in the thoracic region. For static measures of vertebral position, computerised tomography (Kouwenhoven *et al.,* 2006; Fujimori *et al.,* 2012) and ultrasound imaging have been used (Suzuki *et al.,* 1989; Burwell *et al.,* 1999). For dynamic active motion analysis, a thoracic rotation device (Barry *et al.,* 1987), non-invasive electromagnetic system (Willems *et al.,* 1996; Theodordis and Ruston, 2002), SpinalMouse®, a skin surface device (Mannion *et al.,* 2004) and digital photography with a computer analysis programme (Harrison *et al.,* 2007) have all been reported in the literature. The merits of each approach are presented in the following section.

The most basic measurement tool, developed by Barry *et al.* (1987), crudely measured global thoracic rotation using a mounted protractor on a vertically orientated T-frame from a stable base in sitting. Although subjectively this was reported to have measurement reliability (r=0.86 – as measured on one day), no reference was made to the sensitivity of a 'protractor' for

measuring regional mobility, or its validity. Using a similar idea, Johnson et al., (2012) developed this approach further to investigate the reliability of thoracic axial rotation with five testing positions (sitting with wooden pole in front, sitting with wooden pole behind, quadruped position and half kneeling with wooden pole in front and back). Using a sample of 46 healthy subjects, all positions exceed intraclass correlation coefficient ICC $(_{2,3})$ values of 0.81 with half-kneeling right rotation (bar behind) recording highest levels of reliability with ICC $(_{2,3})$0.91, 95% confidence interval of 0.84-0.95. However these results, whilst promising use four testing positions that few older subjects could comfortably adopt. It is of note that seated rotation, the position used most widely in motion analysis, with pole in front was found to have between-day ICC $(_{2,3})$ 0.84 95% confidence interval 0.72-0.91).

A new skin surface measurement instrument, the SpinalMouse®, has been developed to provide a measure of spinal curvature and motion analysis of the spine in the sagittal plane (flexion-extension) (Mannion *et al.,* 2004). However, this tool has not been validated for axial rotation motion analysis.

Computerised Tomography scanning has been used to analyse static vertebral rotation in the thoracic spine from T2-L5 (Kouwenhoven *et al.,* 2006) and T1-T12 (Fujimori *et al.,* 2012). However given computerised tomography requires that subjects are supine and static, and would not be suitable for the evaluation of active range of motion given the ethical issues with radiation exposure and inability to measure active functional range of motion.

A non-invasive low-frequency electromagnetic system (3-Space Fastrak System, Polhemus Incorporated) has been used in a number of studies to evaluate different active movements in the thoracic and cervical region (Culham *et al.,* 1994; Willems *et al.,* 1996; Jordan *et al.,* 2000; Theodoridis & Ruston, 2002). The system uses sensors (up to 4) that are not attached to the base unit allowing free motion of the region to occur. Culham *et al.* (1994) used this system to

measure rib mobility with motion sensors placed anteriorly, posteriorly, and laterally on the thorax in a sample (n=15) of women with osteoporosis and (n=15) a control group. However, this was a global analysis linked to chest wall motion (vertical rib excursion, lateral expansion, *etc*.) and did not specifically investigate range of spinal motion and the use of skin sensors does not overcome the soft tissue artefact. Theodoridis & Ruston (2002) subsequently used this system to evaluate coupled motion (movement occurring in more than one plane) at one thoracic vertebral level during single arm elevation. From a research perspective, reliability of the system as a motion analysis approach has been reported as favourable with inter-observer, intra-class coefficients correlation for all the cervical spine movements ranging from 0.61 to 0.89 $p<0.05$ (Jordan *et al.,* 2000). Caution should be exercised before extrapolating these findings into motion analysis in the thoracic region, given the marked differences of available range of motion in the cervical and thoracic regions.

Partly to overcome the problem of soft tissue artefact and making use of advanced motion analysis systems, ultrasound is increasingly being used to advance our understanding of biomechanics. Ultrasound equipment provides a safe and cost effective means of research. As clinicians further develop advanced practice skills, to include sonography, one could see such technologies moving into clinical practice. Ultrasound technologies for use in motion analysis come in two forms, ultrasound -based motion analysis or ultrasound imaging of bone in conjunction with motion analysis systems.

3.3.1. Motion analysis systems

A three-dimensional ultrasound-based motion analysis device that does not utilise imaging has been used widely for studies of active cervical spine mobility [Natalis & Kinig, 1999 (abst); Dvir & Prushansky, 2000; Perret *et al.,* 2001; Strimpakos *et al.,* 2005], although it has not yet been used for the thoracic or lumbar spine regions. From the literature, it is proposed that the system, which has been validated against x-ray, is considered to be the gold standard for cervical

flexion and extension (Strimpakos *et al.,* 2005), and it is suitable for use in clinical practice. However, it is not known whether it is sensitive enough to accurately measure changes in a spinal region with significantly smaller ranges of motion.

3.3.2. Ultrasound imaging

Whilst ultrasound imaging has not been used for dynamic motion analysis in the spine, it has been used to measure static positional rotation of vertebrae in subjects with idiopathic scoliosis (Suzuki et *al*., 1989; Burwell et *al*., 1999; Kirby *et al*., 1999). With the subjects in prone lying, a measure in degrees of the vertebral position relative to the horizontal plane was acquired using an inclinometer attached to the ultrasound transducer image of the laminae of each level in the spine (being representative of vertebra position) (Suzuki *et al*., 1989; Burwell *et al*., 1999; Kirby *et al*., 1999). Use of ultrasound enhanced the sensitivity and specificity for the detection of scoliosis by 16% and 23% respectively (Burwell *et al*., 1999). Furthermore, measures of laminar rotation obtained correlated statistically significantly with the vertebral rotation obtained using x-ray, despite different test positions being used. Vertebral rotation using this approach was shown to be measured to within ±3.1° (Kirby *et al*., 1999). Although authors suggest that, for regions with increased spinal lordosis or kyphosis, values for rotation may be inaccurate, it does provide a viable alternative to existing approaches with visualisation on the bone overcoming the issue of soft tissue artefact. Several subjects in the study by Suzuki *et al.* (1989) also had computerised tomography performed (not as part of the study, but for other reasons), but the authors made no further reference to this, nor did they perform any correlation analysis between the two methods (ultrasound and computerised tomography) that would strengthen any conclusion that could be drawn about this approach.

In order to move the body of motion analysis research forward, it is essential that the key threat to validity, soft tissue artefact, be quantified. Quantifying soft tissue artefact in the thoracic region could serve to strengthen conclusions drawn from motion analysis studies in the event

there is little soft tissue artefact as a source of measurement error. Or, where considerable soft tissue artefact is found, further consideration should be given to the development of motion analysis approaches that use imaging of the underlying bone.

Two studies have previously reported soft tissue artefact in the thoracic region. Firstly, Yang *et al.* (2005) explored the validity of surface motion analysis in the thoracolumbar region of the spine in osteoporotic subjects (n=31, age 72±4 years) during active sagittal plane motion. Radiographic images (lateral view) were acquired in neutral, full flexion and extension, with motion analysis skin sensors *in situ* to enable a comparison of approaches using different sensor placement. Three skin sensors were placed between vertebral levels T7 and S1 and the accuracy of the skin sensors was measured against the radiographic image data. From full flexion to extension, soft tissue artefact in the thoracic region was reported as 4.23±33.59 mm. This large standard deviation may be attributable to the nature of the sample, being older, with a mean age 72±4 years and osteoporotic, where validity of palpation linked to skin sensor placement has not been established. Whilst this provides evidence of an approach to soft tissue artefact quantification, the external validity of these findings is limited, due to the age of the sample and with most motion analysis studies using young adults.

Zhang *et al.* (2003) also developed an approach to quantify soft tissue artefact using a mathematically generated model and skin surface markers. Although the primary aim of this study was to determine soft tissue artefact in the lumbar spine, the researchers also included markers for the T7 and C7 vertebrae. From preliminary analysis, a measurement error of 3±1.75 mm was reported at the T7 level during flexion in the sagittal plane. However, concern by the authors of the study about the reliability of these measures at T7 resulted in no further analysis being performed on data from these points. Details were not given to fully appreciate concerns raised.

Whilst both these studies considered the soft tissue artefact in the thoracic spine during forward flexion movements, the main motion of interest in this region is axial rotation, with all thoracic spine motion analysis studies using a supported seated position to limit associated lumbar spine motion (Willems *et al.,* 1996; Theodoridis and Ruston, 2002; Edmondston *et al.,* 2007).

The primary aim of this study was to describe soft tissue artefact as a first attempt in quantifying this unknown source of measurement error during axial rotation, the most widely researched movement in the thoracic spine. A secondary aim was to investigate whether an association exists between the ranges of thoracic rotation and the extent of skin displacement.

3.3.3. Methods

A convenience sample of asymptomatic participants was recruited, based on a power calculation using data from a previous study (Zhang *et al.,* 2003), for a 5% significance level powered at >0.9. Subjects with known current or previous musculoskeletal spine conditions, or who had scarring from abdominal surgery, were excluded. Given the nature of the exclusion criteria and that much of the research into motion analysis has been done in young adults, (e.g. aged 18–24 years (Willems *at al.,* 1996), aged 18-43 years (Edmondston *et al.,* 2007; Sizer *et al.,* 2007) a population of young adults were approached to participate in the study. Ethical approval was gained from the School of Sport and Exercise Sciences Research Committee, with all subjects giving informed consent.

3.3.4. Measurement tool and technique

An ultrasound image of the subjects' spinal lamina bilaterally was acquired using a Phillips Sonos 5500 with a 26 mm linear array transducer with a frequency range of 3-11 MHz (Figure 8).

To measure thoracic rotation, the position and azimuth orientation (motion around a vertical axis) of the ultrasound transducer (using x-, y-, and z-coordinates) was acquired and recorded using the Polhemus (Liberty™) motion analysis system (Colchester, Vermont, USA). This laboratory-based, coordinate motion analysis system allows movement to be measured with six degrees of freedom, where the static accuracy is reported as 0.03 inch in root mean square for x-, y- or z-position and 0.15 degrees root mean square for sensor orientation (Polhemus, Liberty™, 2007). The system includes a source transmitter and a sensor. The sensor was fixed to the ultrasound transducer and the source transmitter was placed in a standardised mounted position in front of the subjects. To avoid interference between the sensor and the ultrasound transducer, the sensor was attached on a plastic extension arm that was secured on the body of the transducer

Ultrasound imaging of thoracic vertebrae allowed for visualisation of bone underlying skin. Training in the use of ultrasound imaging was provided and verified by a qualified musculoskeletal sonographer prior to the start of the study. Soft tissue motion was measured using electronic digital callipers, which are accurate to ± 0.02 mm (model ST-089, Maryland Metrics, Owings Mills, MD).

A strand of cotton was fixed across the centre of the ultrasound transducer head to provide an acoustic shadow on the image. An ultrasound image of the spinal laminae at T1, which corresponds with the C7 spinous process (Geelhoed *et al.,* 2006) was acquired. The image was acquired in the horizontal plane on the ultrasound monitor, using reference lines on the monitor (Kirby *et al.,* 1991). This enabled the researcher to acquire a standardised image of the vertebra throughout the study, where the shadow of the cotton intersected the C7 spinous process and the laminae were horizontal.

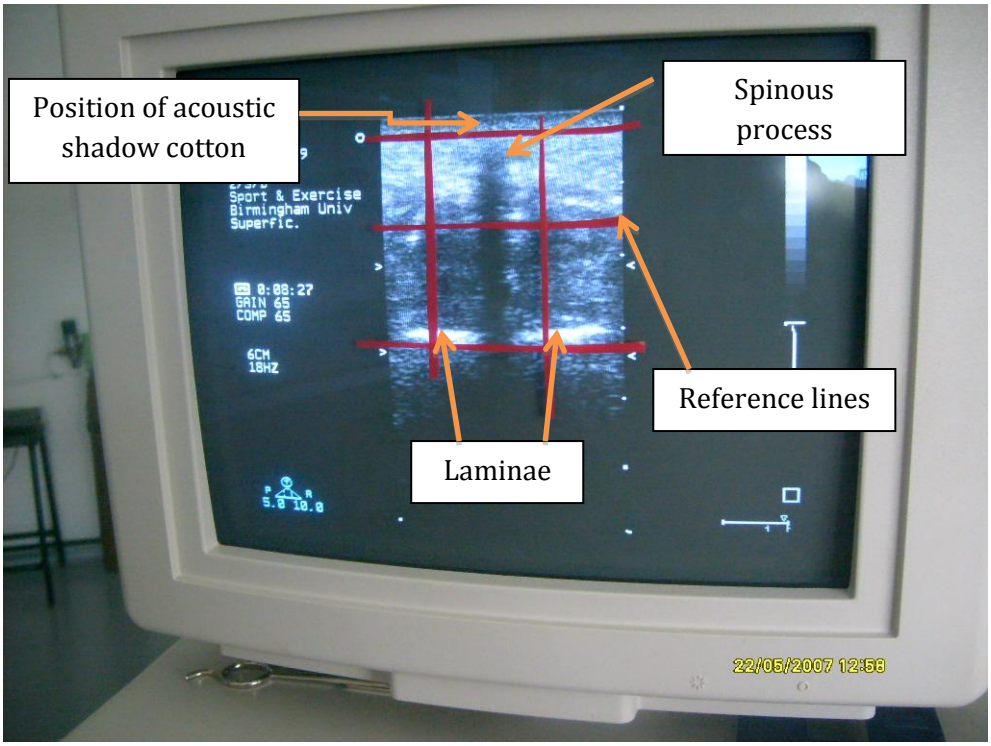


Figure 8. Ultrasound image of spinal vertebrae with laminae clearly visible

3.3.5. Procedure

Familiarisation of the movements of thoracic axial rotation in a standardised seated position preceded the data collection. The lumbar spine was positioned in a neutral position (mid-point between full lumbar spine flexion and extension) and a bar was positioned with its superior surface level with the L1 spinal vertebra to limit movement to the thoracic spine (Edmondston *et al.,* 2007). Additional fixation was achieved using a seatbelt to strap the thighs to the seat. It was originally planned to fixate the lower torso to the vertical struts of the backrest, however during development of the study, it was evident that this caused some discomfort in the lower abdomen during testing. Participants were requested to maintain the contact between their lower spine and the bar throughout testing. Verbal feedback was provided to ensure compliance with the testing procedure.

Palpation of the spinous processes of C7, T5, and T11 vertebrae was performed by the author, an experienced manual therapist. The skin was marked at those vertebral levels using a fine tipped hypoallergenic skin marker. Repeatability of manual palpation at the level of T6 has previously been shown to be good using repeated measures analyses of variance ($F=2.09$, $p=0.161$) for experienced manual therapists (Billis, *et al.,* 2003).

Following instruction and a standardized period of familiarization, subjects moved actively from neutral to a position of full right rotation with their arms folded across the chest to reflect a body position used previously (Willems, *et al.,* 1996). An ultrasound image was acquired as described above, at the end of the subjects' active available range of motion. Then the position of the superior face of the transducer, level with the cotton, was marked on the skin. Subjects returned to neutral spine position, and the distance between the skin marks was measured three times using digital callipers. The soft tissue artefact (mm) was calculated from the mean of these three measurements. Calliper measurement was done in neutral to minimise a potentially inconsistent effect of soft tissue creep (elongation of tissue in response to prolonged loading) at the extreme of the axial rotation. The ultrasound transducer was removed from the skin during each movement to avoid influencing the skin movement over the underlying bone. This procedure was repeated for vertebral levels T6 and T12. This procedure was repeated for T1 left rotation, T6 and T12 right and left rotations. Range of axial motion was measured using a Polhemus (Liberty ™, Colchester, Vermont, USA) motion analysis system whereby a motion sensor was fixed to the transducer and motion around the y-axis recorded and its position recorded at the end of each movement.

3.3.6. Data analysis

Individual and group data were analysed to derive the group mean ranges of left and right rotation (degrees) from the neutral position at each level (T1,T6,T12) and the mean soft tissue artefact (mm) calculated for each motion from the three measures. The range of left and right

rotation (degrees) and mean skin displacement (mm) for each motion are presented descriptively with standard error of the means (SEM).

For the purpose of correlation the criteria set out by Pett (1997) was used, where values between 0.00 and 0.25 indicate weak or no association, values between 0.26 and 0.50 indicate a low degree of association, values between 0.51 and 0.75 indicate a moderate to strong degree of association and values between 0.76 and 1.00 indicate a very strong degree of association.

3.3.7. Soft tissue artefact and range of motion

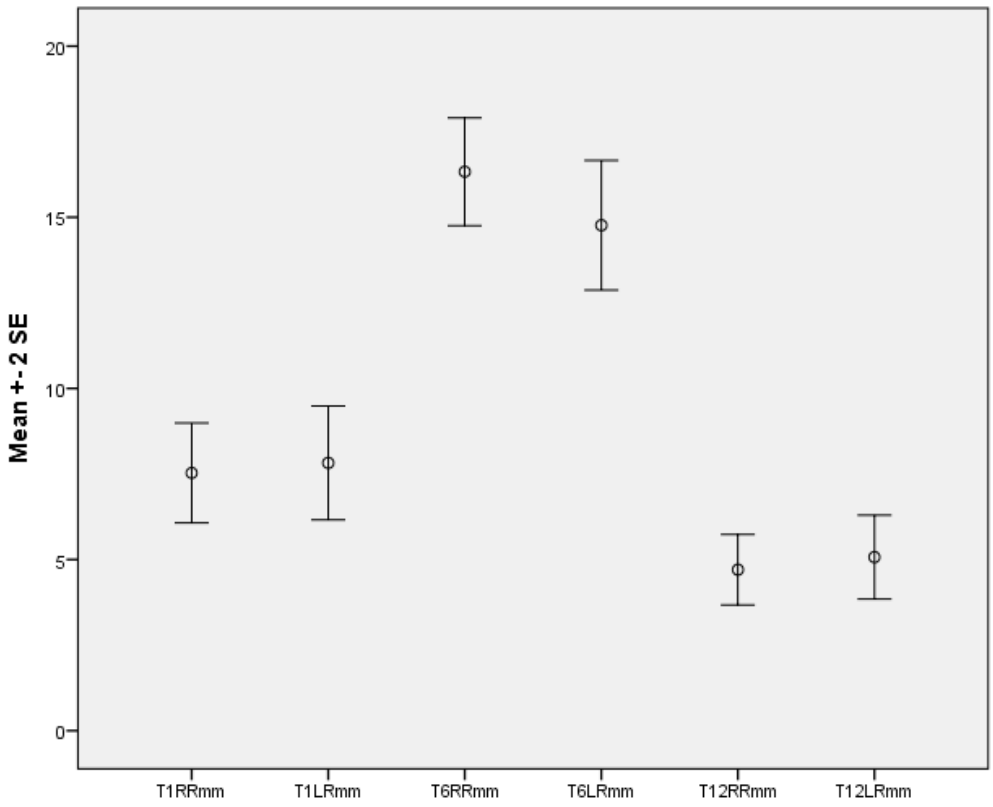
To determine any possible association between range of motion and soft tissue artefact at each level, Pearson product correlations (2-tailed) were performed, where $p < 0.05$. All data analysis was performed using SPSS version 16.00.

3.3.8. Results

The sample included 14 male, 16 female, and age range 18-32 with a mean [(standard deviation (SD)] age 23.83 years (3.1), weight 72.4 kg (14.35), height 171.8 cm (6.6), body mass index (BMI) 21.1 (3.4). The group mean, SD and SEM for each range of motion and soft tissue artefact at each level are shown below in table 7. Soft tissue artefact was found to be greatest in the mid-thoracic region, although range of motion did not differ greatly from the upper thoracic region. Figure 9 illustrates the soft tissue artefact for all movements.

Table 7. The group mean soft tissue artefact (mms) and range of motion (ROM) at each spinal level.

Level	STA (mm)	SD	SEM	ROM (degrees)	SD	SEM
T1 Right rotation	7.93	3.95	0.73	36.11	5.77	1.07
T1 Left rotation	7.75	4.18	0.78	38.51	6.19	1.15
T6 Right rotation	16.57	4.09	0.76	35.03	6.85	1.27
T6 Left rotation	14.96	4.94	0.92	35.66	9.97	1.85
T12 Right rotation	5.11	3.51	0.65	6.53	3.07	0.57
T12 Left rotation	5.02	3.07	0.57	6.62	3.57	0.66



RR; right rotation, LR; left rotation

Figure 9. Soft tissue artefact (mm) and range of motion for each level are presented. Most soft tissue artefact occurred in the mid thoracic region, irrespective of the range of thoracic rotation.

An association of moderate strength was found between soft tissue artefact and range of motion was found for the mean group data for T6 left rotation, and T12 left rotation, r=0.52; r= 0.52 ($p < 0.001$) respectively. However T1 right rotation (r=0.12), T1 left rotation (r=0.11), T6 right rotation (r=0.23), T12 right rotation (r=0.03) showed no meaningful evidence of an association. Overall however there was no evidence of an association between soft tissue artefact and range of motion, the implications of which are discussed in the next section.

3.3.9. Discussion

The aim of this study was to describe soft tissue artefact during active thoracic axial rotation. The results show that soft tissue artefact varies considerably within the thoracic spine, with most soft tissue artefact occurring in the mid thoracic region.

Whilst other research has reported soft tissue artefact in the thoracic spine (Zhang *et al.,* 2003; Yang *et al.,* 2005), comparisons between studies are impossible due to different movements being used. Collectively these studies, along with the current study, do provide evidence that soft tissue artefact is a source of measurement error using methodologies that utilise skin-mounted sensors.

The findings from this study suggest that the region with greatest soft tissue artefact is the mid-thoracic region, irrespective of relative ranges of motion. This could, in part, be explained by the use of a sitting posture with the arms folded across the chest, because there may be greater tension on the overlying soft tissue. Given axial rotation is the movement of most interest, quantification of soft tissue artefact in sitting is important. Using a seated position enables subjects to move through the full available range of motion as used in previous studies (Willems *et al.,* 1996). More recently, Edmondston *et al.* (2007) tested subjects in sitting with arms in a position of mid-abduction as a means of standardising the test procedure, although this would provide standardisation it is neither functional nor practical for older adults.

Range of axial motion was measured to evaluate whether a linear relationship exists for range of motion and soft tissue artefact. Had the extent of skin displacement be associated with the magnitude of range of motion, this source of measurement error could potentially then be compensated for during the analysis of the data derived from approaches that use skin sensors. However as this was not the case, correlations were simply reported and no further consideration was given to this. Whilst the magnitude of the artefact relative to range of motion

was greatest at the T12 level, the extent of the artefact was in fact very small (~5 mm) and therefore no further consideration was given to this.

The values for soft tissue artefact reported in this paper may, in fact, underestimate the 'true' soft tissue artefact, as the calliper measurements between the skin marks were done with subjects in their neutral spine position. This was to minimise the potentially inconsistent effect of soft tissue creep and muscle activation levels at end range positions through hysteresis. It was noted by the researcher that the elastic recoil of the skin and associated underlying soft tissues led to the marks approximating from their 'absolute' position at the end of axial rotation, especially at the T6 level.

An issue not explored in this study was the variability of soft tissue artefact at different bony landmarks of the vertebrae or where dermal thickness may vary between subjects. Soft tissue artefact has previously been reported to be greater in places where soft tissue thickness is greater, such as over the transverse processes (Cervari *et al.,* 2004; Gao & Zheng, 2008).

Future studies using skin-based motion analysis sensors also need to consider the possibility of an additional threat to validity arising from the relative motion between the skin sensors and the skin. Whilst this was not measured in this study, future research could evaluate this using skin sensors in conjunction with imaging technologies, as has been performed in other motion analysis systems (Stagni *et al.,* 2005).

Whilst many attempts have been made to compensate or minimise soft tissue artefact during the use of skin sensor based motion analysis research (Leardini *et al.,* 2005), soft tissue artefact continues to pose a threat to the validity of findings. Perhaps the solution is to use these systems in conjunction with imaging technologies, such as ultrasound (Patel *et al.,* 2004), that have become more widely available and less costly in recent years. Establishing criterion-related

validity of the methodological approach used in this study, against x-ray imaging, considered the gold standard for motion analysis testing to measure range of motion would strengthen the conclusions that could be drawn from this study. However, using ultrasound imaging allows for visualisation of the underlying bone to enable soft tissue artefact to be measured, offering face validity to this methodological approach. Future research could also seek to establish the reliability of this approach and to utilise different samples to increase the findings' generalisability to other populations.

3.3.10. Summary

This study describes soft tissue artefact during thoracic axial rotation using ultrasound imaging of bone and motion analysis to quantify range of motion. The region of greatest soft tissue artefact was found in the mid-thoracic region during axial rotation, providing evidence to support the development and use of imaging technologies, in conjunction with motion analysis, as a means of minimising this source of measurement error in spinal motion analysis research.

Chapter 4. STABILITY AND INTRA-TESTER RELIABILITY OF AN IN VIVO MEASUREMENT OF THORACIC AXIAL ROTATION USING AN INNOVATIVE METHODOLOGY

Publication

Heneghan NR, Hall A, Hollands M, Balanos GM. (2009) Stability and intra-tester reliability of an in vivo measurement of thoracic axial rotation using an innovative methodology. Manual Therapy 14(4):452-455. (Appendix 6)

4.1. Abstract

Purpose: The aim of this chapter was to evaluate measurement properties of an innovative approach to evaluate active thoracic spine axial rotation in a functional seated position: measurement of the stability and intra tester reliability.

R**elevance:** Research into the effectiveness of clinical interventions, such as manipulation requires valid and reliable outcome measures. Many published studies that purport to measure thoracic movement rely on surface electrodes/sensors. Several factors including movement between the sensor and skin, and skin and bony prominences compromise the reliability and validity of existing measures.

Participants: Based on 5% significance level with reliability (ICC $_{2,1}$) powered at >0.8, a convenience sample of young healthy adults (n=24) (9 male, 15 female) with a mean (SD) age 24.96 years (2.6) was recruited. Exclusion criteria included: current / previous neuromusculoskeletal spine condition, systemic rheumatological condition, history of abdominal surgery, risk of being / being pregnant, current / chronic respiratory dysfunction

Methods: A prospective, test-retest, intra tester reliability study to establish the within and between day intra tester reliability of thoracic axial rotation in sitting (lumbar spine neutral) using motion analysis combined with ultrasound imaging. An image of T1 spinal lamina was acquired horizontally on the ultrasound monitor and a coordinate position (Cartesian) of the US transducer was recorded. The change in coordinate position around the vertical axis was then recorded for full right and full left active rotation on ten consecutive repetitions (trial 1) where T12 was fixed using a bar. This protocol was repeated again on the same day (trial 2) to provide data for within day reliability and 7-10 days later (trial 3) for between day reliability.

Analysis: Stability was determined using descriptive and inferential data analysis on the ten measures of axial rotation (in degrees) across trial one using a combination of standard deviation (SD), standard error of means (SEM), coefficient of variation (CV) and repeated measures ANOVA

Intra-tester reliability was determined using ICC ($_{2,1}$) with $p<0.05$ confidence interval (CI). Bland Altman plots were drawn to plot % agreement of measures at 95% CI (trials 1&2, 1&3).

Results: The mean total range of axial rotation was 85.15-degrees across a single trial with SD=14.8, SEM=3.04, CV=17.4. SEM ranged 0.63-3.37 for individual subjects and 2.60-3.64 across repetitions. Stability of performance occurred at repetitions 2-4. Intra-tester reliability (ICC $_{2,1}$) was excellent within day (0.89-0.98) and good/excellent between days (0.72-0.94).

Conclusions: The results from this study indicate that stability was achieved and intra-tester reliability of this innovative approach is good to excellent for within and between days respectively. This measurement tool could be employed to measures thoracic range of axial rotation in a young adult population. Further work is required to investigate the inter-tester reliability, validity and application in different populations.

4.2. Introduction

Having quantified and reported soft tissue artefact of ~30 mm (16.57 + 14.96 mm soft tissue artefact at level of T6: see table 7) in the mid thoracic region during full axial rotation of young adults in Chapter 3, the need to develop an alternative measurement tool, not involving skin sensors was evident. Ultrasound imaging is widely used as a clinical and research tool because it is safe and relatively inexpensive. The purpose of this study was to evaluate a novel approach to the measurement of thoracic spine axial rotation using ultrasound imaging in conjunction with motion analysis.

For an approach to be a viable option for this measurement, it needs to be evaluated in terms of its stability over repeated measures and reliability. Stability considers how consistent a tool is at producing a result whilst measuring the same entity on repeated occasions (Sim & Wright, 2000). Owing to the viscoelastic properties of tissues (stress relaxation and hysteresis), range of motion may increase with increasing repetitions. Stress relaxation being time-dependent decrease in stress under load and hysteresis being energy lost through a loading cycle. Once stability of measures is established, reliability, which is fundamental to evidence-based practice, may be investigated. Within- and between-day reliability provides an indication of how useful a method is in detecting change in motion following clinical interventions such as manipulation.

4.3. Materials and methods

A prospective test-retest design combined an evaluation of stability with a within- and between-day intra-tester reliability.

A convenience sample of asymptomatic subjects (n=24) was recruited, based on a power calculation based on a 5% significance level with reliability ($ICC_{2,1}$) powered at >0.8 requiring n≥19 (Walter *et al*., 1998). The sample included 9 males and 15 females, age range of 18-32 years with a mean (SD) age 24.96 years (2.6), weight 70.8 kg (14.35), height 170.2 cm (8.7). A

combination of factors informed the decision to use a sample of young adults during the evaluation of this measurement approach including, the need to take repeated measurements to calculate stability of the measure; take measurements on multiple occasions (originally 3 occasions) to evaluate reliability and to minimise the influence of extraneous factors which may impact on the study of stability and reliability, such as fatigue, degenerative changes in the spine *etc.*

Ethical approval from the School of Sports and Exercise Sciences, University of Birmingham, was gained with all participants giving informed consent.

Participants were excluded if they had a current or previous neuromusculoskeletal spine condition, a pre-existing systemic rheumatological condition, had undergone abdominal surgery, were pregnant, or were affected by a current or chronic respiratory condition.

4.3.1. Equipment

An ultrasound image of the subjects' spinal lamina bilaterally was acquired as described earlier section (3.3.4) using a Phillips Sonos 5500 with a 26 mm linear array transducer with a frequency range of 3-11 MHz. The position and azimuth orientation was determined and recorded using the Polhemus (Liberty™) motion analysis system (Colchester, Vermont, USA). As described earlier the motion sensor was fixed to the ultrasound transducer and the source transmitter was placed in a standardised mounted position in front of the subjects. To avoid interference between the sensor and the ultrasound transducer, the sensor was attached on a plastic extension arm that was secured on the body of the transducer (Figure 10).

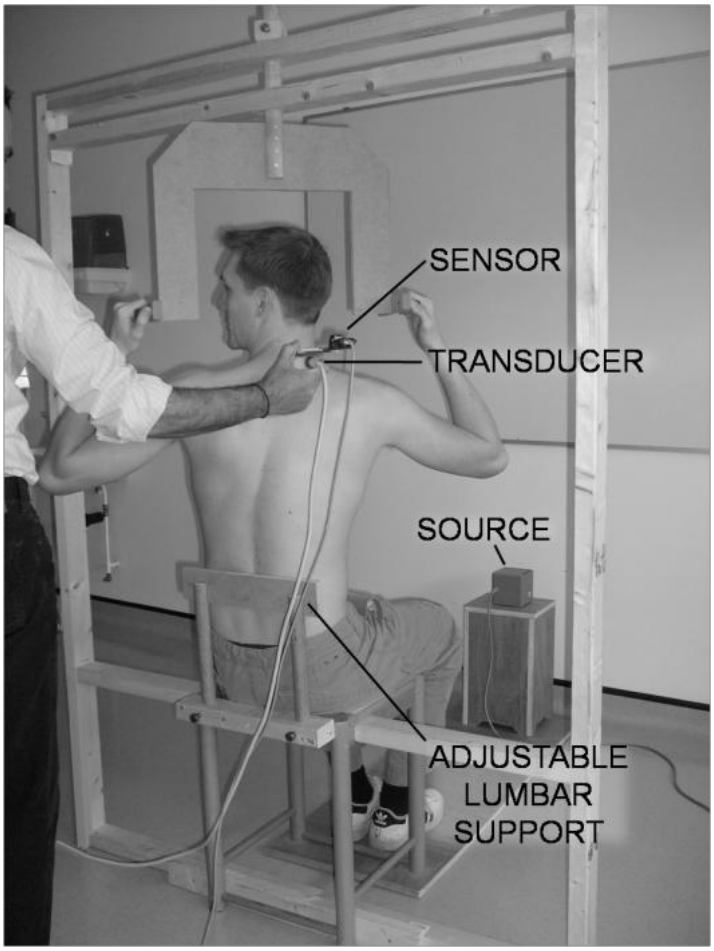


Figure 10. Experimental set up for motion analysis.

4.3.2. Procedure

A pilot study determined the feasibility of the test protocol. This resulted in the following modifications being made to the protocol and procedure:

- The experimental rig was adapted to include an overhead bar and handles for participants to hold onto to as a means of standardising spinal position across trials.

- A self-adhesive foam pad was placed on the seat to increase the friction between participants' thighs and the seat and minimise movement on the seat.

- Subjects were reluctant to commit to testing on three separate occasions; the protocol was adjusted to limit attendance to just two occasions which allowed within day and between day analyses to be evaluated.

Subjects were seated in a standardized position using a custom made wooden frame with their lumbar spine secured (seatbelt across thighs) and stabilised in the neutral position (pelvis and lumbar spine mid-way between the extremes of motion in the sagittal plane), their legs fully supported with hips and knees at 90-degree angle and their arms in mid-abduction (Figure 10). A fully adjustable wooden bar was positioned at the level of the LI vertebra with the aim of minimising movement at the lumbar spine. This position was used to standardise thoracic spine posture across repetitions and trials, as posture has been shown to influence thoracic motion (Edmondston *et al*., 2007).

Familiarisation of the procedure with movement of the head preceding thoracic spine motion was performed with a demonstration and standardised short warm up of 10 repetitions, where subjects avoided the extremes of right and left rotation. This standardised warm up process was repeated for a single follow up, 7-10 days later.

The spinous process of the C7 vertebra was palpated in the neutral position and the skin at that location was marked. An ultrasound image of the T1 spinal laminae was acquired in the horizontal plane on the ultrasound monitor using horizontal and vertical reference lines on the ultrasound monitor (Figure 11). The coordinate position of the transducer was then recorded. The participant actively moved to a position of maximum axial rotation and maintained the position whilst a 'new' image of the T1 spinal laminae was acquired and the 'new' transducer position recorded. Measurement of thoracic spine rotation was determined from the data acquired for end range position of the T1 vertebra, with motion occurring around the y-axis.

With the lumbar spine supported or 'fixed' one can infer that all movement occurring above T12 will be represented by the end range position of T1.

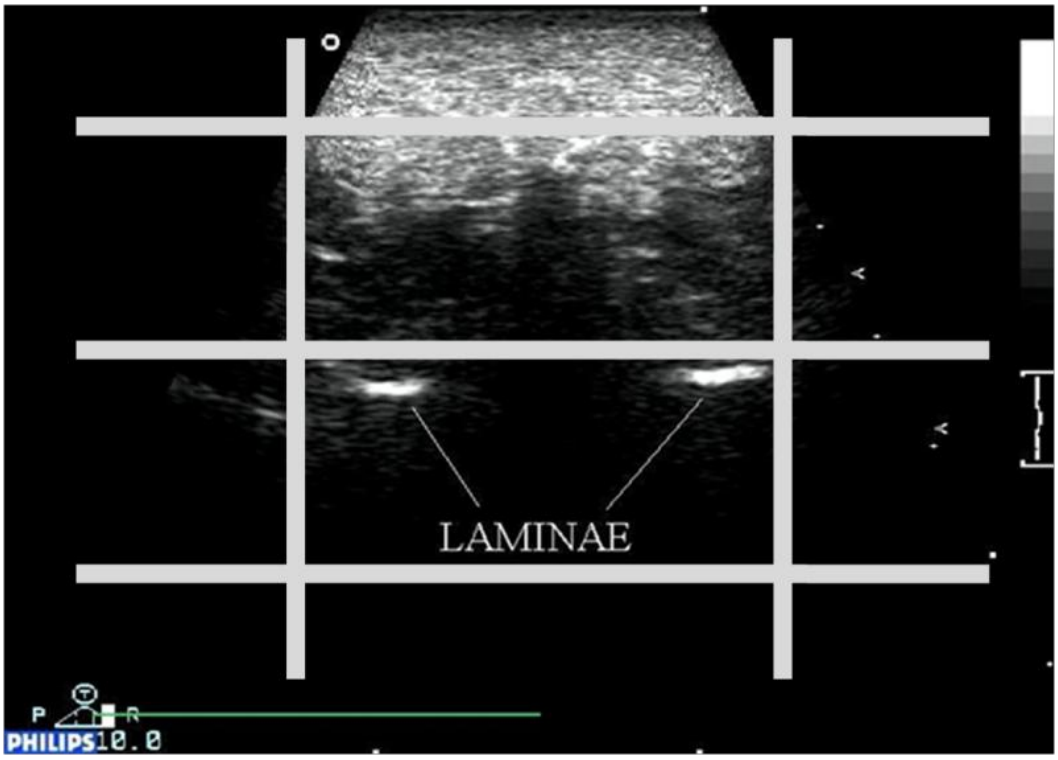


Figure 11. Ultrasound image of laminae in relation to reference lines on the monitor screen

The minimal acceptable criteria for each image was that the C7 spinous process and T1 laminae had to be clearly visible and consistent on each occasion with respect to their position on the monitor relative to the reference lines.

This procedure was done sequentially starting from the neutral position, to full right rotation, returning to the neutral position and to full left rotation for ten consecutive repetitions for a single trial. Although data was captured for transducer movement about the x- and z- axes, this study only used data from the y-axis to calculate thoracic axial rotation. The transducer was removed from the skin following each data point to avoid any influence on the subjects' active

motion. Expertise in image acquisition was required to minimise stress relaxation, which may occur with prolonged holding at end-range positions.

Each participant attended on two occasions to perform a total of 3 trials. Trials 1 and 2 took place on the first occasion and subjects were allowed to get up and move about 10 minutes between trials. Trial 3 took place 7-10 days later with environmental and diurnal variables, such as temperature and lighting being controlled for. Data analysis took place once all measurements across all three trials had been recorded.

Accuracy of the Polhemus (Liberty™) motion analysis system (Colchester, Vermont, USA) system was evaluated using the method described by Koerhuis *et al*., (2003) using a 'mock' spine. A rod with the ultrasound transducer fixed at the top of the unit was mounted on a stand. The transducer, with a motion sensor attached, was then axially rotated (across a 180-degree range, 90-degrees to the left and right, 45-degrees to the left and right and neutral position of 0-egrees), including varying positions of tilt (up to 15 degrees) to simulate out of plane motion across 125 trials. Accuracy of the measurement tool was calculated using the mean and standard deviation of the mean absolute error between known angle of 0-, 45-, 90-degrees angle and motion analysis measurement across the trials.

4.3.3. Data Analysis

The individual and group data were analysed to derive the range of rotation to the left and to the right from the neutral position. The range of left and right rotation is presented descriptively with means and standard deviation. A composite measure for full right and left axial rotation for each repetition was then calculated from the raw data and used for subsequent analysis. Utilising a composite score negated the need to return to 0-degrees between testing; participants' neutral position varied by approximately ±8-degrees reflecting individual variability such as asymmetry of spinal vertebrae and the spinal column. All data analysis was

performed using SPSS version 14.00. The level of statistical significance was considered as $p<0.05$.

To assess the stability of measures data from Trial 1 was used, with the individual and group means being analysed descriptively across the ten repetitions. Stability, consistency of a measure over repeated testing, was analysed using means for accuracy, standard deviation for precision, standard error of the mean as a measure of the sampling error, and the coefficient of variation to calculate the variability of repeated measures relative to the mean (Sim & Wright, 2000).

In order to derive a measure for subsequent inferential analysis of reliability, repeated measures one-way ANOVA on successive triads of repetitions across Trial 1 was used (repetitions 1-3, 2-4, 3-5, 4-6 etc). The triad of data where there was least variability within the trial data set using effect size was analysed using a confidence interval of 95%.

Intra-tester reliability analysis, using intra-class correlation coefficients ($ICC_{2,1}$) from a repeated measures ANOVA test, was calculated using 95% confidence intervals to determine the within-day (Trial 1 and 2) and between-day (Trial 1 and 3) reliability. Reliability is deemed to be 'good' where values range 0.61-0.80 and 'excellent' for values between 0.81-1.00 (Shrout, 1998). Limits of agreement analysis (95%) were derived using Bland Altman plots for Trials 1 and 2 (within-day), and for Trial 1 and 3 (between-day) (Bland & Altman, 1986).

Repeatability analysis across all three trials was performed using repeated measures ANOVA on the mean value of the triad with the least variability from Trial 1 and the middle value from this derived triad.

4.4. Results

The mean absolute error or accuracy of the measurement system using the 'mock' spine was calculated to be 1.73± 2.37 degrees, across the 180-degree range (See appendix 7 for raw data).

The mean range of motion for full left and full right rotation across ten repetitions for each trial, including standard deviation and range, were calculated (Table 8). The mean composite range of axial rotation was 85.15 degrees across a single trial (SD=14.8, SEM=3.04, coefficient of variation=17.4).

Table 8. Range of motion for left and full right rotation, including standard deviation.

	Left rotation in degrees (SD)	Right rotation in degrees (SD)
Trial 1	44.06 (8.76)	41.09 (8.01)
Trial 2	43.58 (8.47)	40.63 (8.17)
Trial 3	43.45 (7.49)	41.86 (6.44)

4.4.1. Stability

The data was normally distributed across Trial 1, using a Kolmogrov-Smirnov test ($p > 0.05$). Figure 9 illustrates mean values (±SEM) for each successive repetition across Trial 1. Although the between-subject variability of total axial rotation was considerable (mean SEM = 3.23), within-subject variability across the ten repetitions was rather small (mean SEM = 1.70).

Statistical analysis was performed on the data to determine the triad with the least variability across Trial 1 (Table 9). Repeated measures ANOVA for repetitions 1-3, 2-4, 3-5, 4-6, etc. showed that repetitions 2-4 had the smallest effect size and least variability (partial Eta squared 0.005 at $p=0.95$) compared with all other combinations. On repeating this for trials 2 and 3 stability was deemed to occur for repetitions 1-3 in trial 2 and repetitions 3-5 for trial 3 (Table 9).

Table 9. Trial 1, 2, and 3 results with effect size and p-values for all triads

	Effect size trial 1	**p value**	***Effect size trial 2***	***p value***	***Effect size trial 3***	***p value***
Repetitions 1-3	0.012	0.87	***0.003***	*0.95*	*0.016*	*0.87*
Repetitions 2-4	**0.005**	**0.95**	*0.020*	*0.70*	*0.014*	*0.77*
Repetitions 3-5	0.027	0.74	*0.046*	*0.43*	***0.003***	*0.94*
Repetitions 4-6	0.039	0.64	*0.021*	*0.68*	*0.018*	*0.72*
Repetitions 5-7	0.033	0.69	0.060	*0.88*	*0.057*	*0.35*
Repetitions 6-8	0.136	0.20	*0.049*	*0.40*	*0.054*	*0.37*
Repetitions 7-9	0.049	0.58	*0.070*	*0.27*	*0.109*	*0.13*
Repetitions 8-10	0.049	0.60	*0.070*	*0.29*	*0.150*	*0.05*

Figure 12. Stability across Trial 1 (n=24)

4.4.2. Reliability

Using group mean data from repetitions 2-4 for each trial, the reliability (ICC $_{2,1}$) was shown to be 'excellent' for within-day measures (0.89-0.98) and 'good/excellent' for between-day measures (0.72-0.94), where a value of 0.75 or greater indicates excellent reliability; 0.40 to 0.75, fair to good reliability; and 0.40 or less poor reliability (Fleiss, 1986). Furthermore, analysis of reliability (ICC $_{2,1}$) using only the value from the third repetition of the measurements was also 'excellent' (0.80-0.96) and 'good/excellent' (0.76-0.95) for within- and between-day measures respectively. This therefore supports the use of a warm up of 2 repetitions for this thoracic motion analysis with a single measurement being recorded on the third repetition being appropriate for the purpose of data analysis.

Bland Altman plots illustrate at 95% CI agreement for within- and between-day reliability, Trials 1 and 2, and Trials 1 and 3, with the mean value from the 2-4 repetition for each trial (Figure 13).

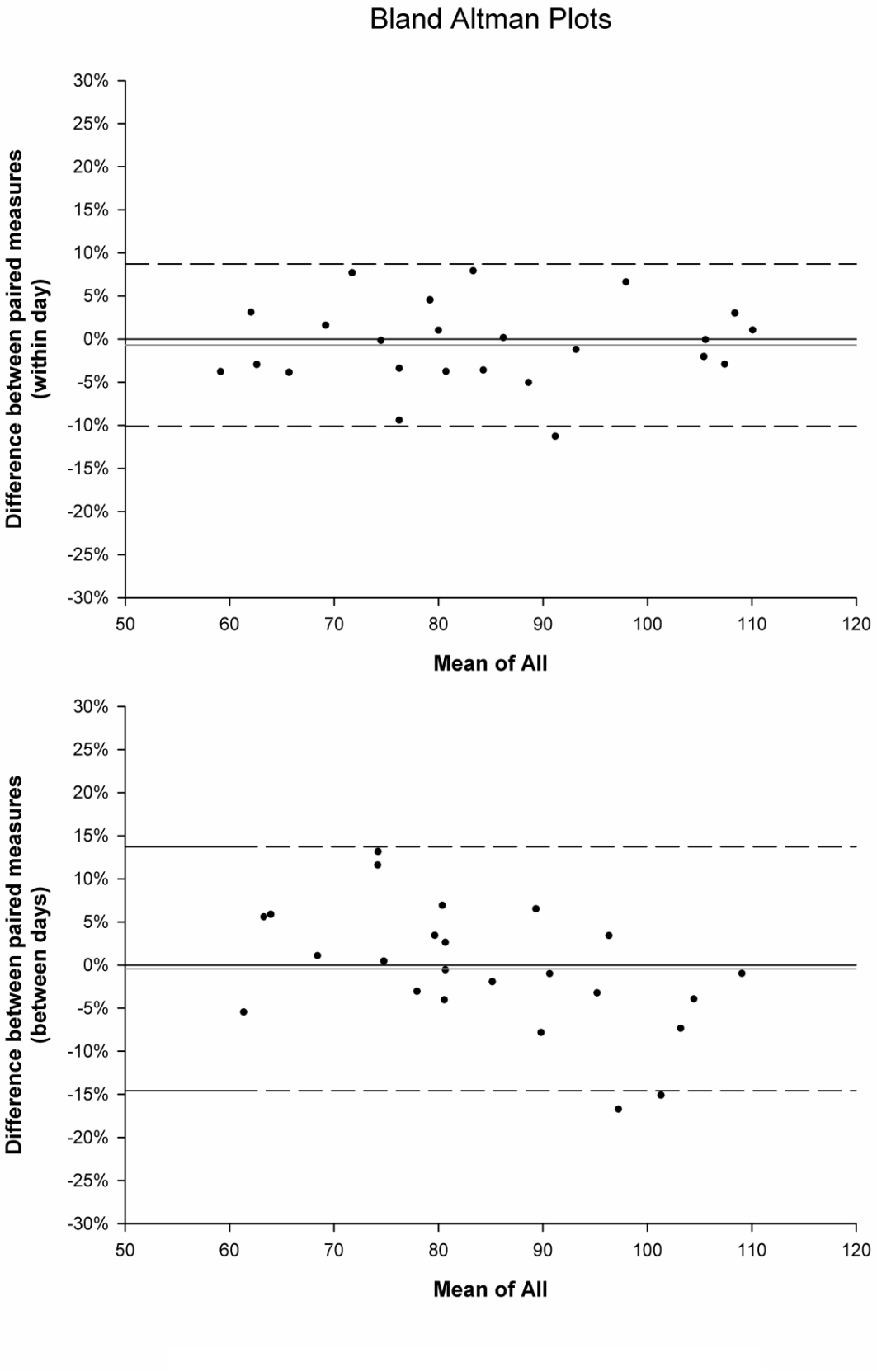


Figure 13. Bland Altman plots for within day (trials 1&2) and between comparisons (trials 1&3).

4.4.3. Repeatability across trials

The repeatability across all trials using the mean value for repetitions 2-4 or the third value was shown to be good (repeated measures ANOVA, $p>0.9$). The mean values were 84.5, 83.8 and 84.0 degrees for Trial 1, 2 and 3 respectively, using the mean of 2-4, and 84.5, 83.8, 83.7 degrees for Trial 1, 2 and 3 respectively, using the value from the third repetition.

4.5. Discussion

The findings of this study suggest that the innovative combination of ultrasound imaging and motion analysis provides a stable and reliable method for the measurement of thoracic rotation in a functional seated position. The basis for the development of this technique primarily relates to the need for reliable evaluation of the effectiveness of clinical interventions in this relatively under-researched region of the spine. Surface markers and sensors, the preferred approach for motion analysis of this region *in vivo* (Willems, *et al*., 1996; Theodoridis & Ruston, 2002; Edmondston, *et al*., 2007), possibly lack accuracy and reliability due to relative movement between the sensor, skin and bone (Willems, *et al*., 1996; Edmondston, *et al*., 2007).

The stability of the measurements appeared reasonably constant, despite some considerable variation between subjects. This may in part be due to the use of a standardised sitting posture, resulting in some individuals performing axial rotation away from their 'normal' sitting posture. The experimental set up was used to ensure that subjects' thoracic posture was consistent across repetitions and trials. Motion in other planes was recorded. However, in this instance, data was only analysed to determine axial rotation. In comparison to the previous study of soft tissue artefact which included motion analysis the range of motion differed slightly with the present study recording a composite range of 85.15-degrees (SD 14.8) and Heneghan *et al.,* (2010) reporting 74.62-degrees in a comparable aged sample. These differences are likely a

consequence of different testing positions, with soft tissue tension limiting the available range of motion when arms are folded across the chest.

Although minimal time was spent at the extremes of the range of motion, stress relaxation may account for the slight trend for increase in range across each trial. Hysteresis may explain the lack of cumulative increase in range from Trial 1 to 2, with tissues having a chance to 'recover' between trials, although recovery times have not been published.

Whilst intra-tester reliability was found to be 'excellent' and 'good to excellent' for within- and between-day measures respectively, using the data from either the third repetition or the mean of the 2-4 repetitions, some caution should be taken when interpreting the results alongside the Bland Altman plots. The Bland Altman plots suggest that the difference between paired measures is up to 10% and 15% for within- and between-day agreements of measures respectively. Given that the mean range of motion was 85-degrees, this suggests there could be an error as large as 8-10 degrees for some subjects. Visual inspection of the graphs, however, suggests that the approach may be better suited for within-day measures, where the percentage difference for the majority of subjects is less than 5%. Further research with a larger sample is indicated to explore the nature and extent of sources of error with this approach and perhaps using images of more than one spinal level.

This is the first study that has utilised ultrasound imaging of the spine in dynamic and functional motion analysis as a means of ensuring that the start and end-body positions and postures are truly representative of the underlying bony anatomy. As image acquisition of sufficient quality is operator-dependent and the motion analysis system and ultrasound equipment reasonably expensive, there is currently little prospect for this becoming a mainstream clinical practice measurement tool. However, as our current understanding of biomechanics and effects of interventions in this region is considerably underdeveloped compared to other areas of the

spine the need to consider alternative non-invasive measurement approaches remains. Future research could explore stability and reliability in different populations, as older tissues are likely to respond differently to repeated movement. With respect to the broader evidence base, further research could explore regional or segmental motion analysis using data from all three coordinates (x-, y-, z-) or evaluate vertebral coupling, which has been debated in this region.

4.6. Summary

Ultrasound imaging, combined with a motion analysis system, has been shown to be a reliable method of measuring active thoracic axial rotation in a seated position. Although the intra-tester reliability of the approach was shown to be "good to excellent", further work would be necessary to establish inter-tester reliability and its applicability for use in different populations for this approach to be more widely adopted.

Chapter 5. DIFFERENCES IN POSTURE, JOINT MOBILITY AND MUSCLE SENSITIVITY IN SUBJECTS WITH AND WITHOUT COPD: AN OBSERVATIONAL STUDY

5.1. Abstract

Purpose: to examine the differences in posture, joint mobility and muscle sensitivity in subjects with COPD compared to a matched group of healthy subjects

Relevance: COPD is widely recognised as a multisystem disease with evidence of changes extending beyond the lung to the musculoskeletal system including bone and muscle. It has been postulated that reduced flexibility in the thorax may be detrimental to pulmonary function, and that techniques to enhance mobility may improve lung health. However previous studies have not examined musculoskeletal differences in subjects with COPD compared to healthy controls. The aim of this study was to examine thoracic mobility (primary outcome) and cervical spinal mobility, posture and cervico-thoracic muscle sensitivity (secondary outcomes) in adults with COPD compared to a matched group of healthy subjects.

Design and Methods: A matched observational study and reported in accordance to STROBE Guidelines. During a single visit, subjects were screened and underwent an assessment by an experienced musculoskeletal physiotherapist. The main exposure measure was assessment of lung function, and the performance-based outcome measures or predictors: posture, joint mobility, and muscle sensitivity. In addition, a number of socio-demographic and other health measures which were potential confounders were assessed through patient report using questionnaires and performance-based measures from physical examination.

Results: The sample comprised participants with COPD (n=33); [mild (n=12), moderate (n=13) and severe (n=6) COPD] and age matched controls (n=55). There was a trend for reduced thoracic and cervical spine mobility, altered cervico-thoracic posture and heightened sensitivity in accessory muscle of respiration in the COPD population. Reduced thoracic axial rotation and altered neck posture were associated with poorer pulmonary function and having diagnosed COPD.

Conclusions: This study provides preliminary evidence to support the inclusion of some flexibility or mobility exercises as an adjunctive intervention aimed at maintaining or increasing flexibility in the thoracic region in COPD. A well-designed, fully powered clinical trial is now required to systematically evaluate the effectiveness of a musculoskeletal flexibility programme

in COPD, using validated patient-reported and performance-based outcome measures with short and long term follow up.

5.2. Introduction

Physical exercise training is a key feature of pulmonary rehabilitation programmes aiming to develop physiological capacity through aerobic exercise, such as walking and stair climbing. Some researchers advocate that flexibility interventions to enhance the biomechanics of breathing (passive manual therapy techniques and active thoracic mobility exercises) should also be considered as a management option for patients with COPD (Paulin *et al,* 2003; Engel & Vemulpad, 2009). As noted from reviews of RMSG evidence (Chapter 1) and evidence synthesis of passive manual therapy (Heneghan *et al.,* 2012), high quality empirical evidence to support or refute this is currently lacking. With physiotherapy guidelines recommending further research into the effects of thoracic mobility exercises in COPD (Bott *et al*., 2009) and the disease now being recognised as a multisystem disease, there is still much to be learned about the effects of COPD on the musculoskeletal system in relation to the mechanics of breathing, such as posture, spinal motion and muscle sensitivity. We have some knowledge of changes to bone and peripheral muscle weakness (Fabbri & Rabe, 2007; Gea *et al.,* 2009), however, this does not cover the breadth of musculoskeletal structures that, through anatomical association, may influence respiratory biomechanics, such as posture or spinal mobility.

A number of studies, discussed in Chapter 1, have described musculoskeletal structural changes among people with COPD, although the influence of such changes on pulmonary function remains largely unclear (Walsh, 1992; Cassart *et al*., 1996; Peche *et al*., 1996; Jorgensen *et al*., 2007; Kjensli *et al*., 2009). Kjensli *et al*. (2009) reported the prevalence of vertebral deformities, based on morphological changes from radiographs, in COPD subjects (n=465) as 31% compared to 18% in a control group (n=462) ($p<0.001$). Using a semi-quantitative approach, deformities were identified using radiographic images. Anterior, mid and posterior heights and

corresponding height ratios of the vertebrae of interest and those adjacent were compared to determine whether or not deformities were present (Kjensli *et al*., 2009). Moreover, they demonstrated an association between higher prevalence of deformities and increasing disease severity in females (Kjensli *et al*., 2009).

The influence of thoracic mobility on pulmonary function in COPD has not been investigated, and, although an evidence synthesis (Heneghan *et al.,* 2012) concluded manual therapy, a passive intervention, exerted little effect on pulmonary function in subjects with COPD (Noll *et al*., 2009), these findings cannot be generalised to other musculoskeletal therapeutic interventions, such as active exercise, and across all presentations of the disease severity. In view of this, and given the complexity of the musculoskeletal system in the thoracic region, an evaluation of the nature of changes in muscle structure/posture and spinal mobility in COPD was necessary. Such knowledge could inform a future clinical trial of active mobility exercises in COPD.

The aim of this study was therefore to examine the differences in posture, joint mobility and muscle sensitivity in subjects with COPD compared to a matched group of healthy subjects. The specific research questions for this study were:

1. How do cervico-thoracic posture, joint mobility and muscle sensitivity differ in subjects with and without COPD?

2. What is the relationship between pulmonary function (as measured primarily by FEV_1) and cervico-thoracic posture, joint mobility and muscle sensitivity in COPD with thoracic motion as a primary measure?

3. Is there an association between cervico-thoracic posture, joint mobility and muscle sensitivity and having diagnosed COPD?

5.2.1. Study Design

This was a matched observational study that utilised a number of clinical assessment tools to evaluate pulmonary and musculoskeletal function among patients with and without COPD. The study was designed and is reported in line with STROBE Guidelines for reporting observational studies (STROBE, 2012) (See appendix 8). Whilst a steering group was not formally convened, the proposal, protocol and selection of measures was extensively discussed and refined following consultation with a number of stakeholders. These included a consultant respiratory physiotherapist with expertise in COPD, a GP, respiratory consultant at University Hospital Birmingham, British Lung Foundation representatives and two patients.

5.2.2. Setting

COPD subjects, with a diagnosis of COPD, were recruited from outpatient respiratory clinics (n=2), local GP clinics (n=2), pulmonary rehabilitation groups (n=3), and Breathe Easy support groups from the British Lung Foundation (n=3). Control subjects, with no diagnosis of COPD, were recruited from the same sources, as many partners or family members were interested in offering support as well as a data base of older adults held within the University of Birmingham, University personnel and word of mouth. Additional control subjects were invited to participate from local activity groups in Birmingham. Recruitment and testing took place between May 2010 and August 2011.

5.2.3. Study population

A convenience sample of subjects with stable COPD and an age (within +/- 5 years) and a matched control group of healthy subjects were recruited through the same sources described above with COPD subjects being approached first and matching (age and gender) of controls in parallel from the sources and database. Inclusion criteria included having a diagnosis of stable COPD (as per NICE Classification, 2004) and ability to speak English. Subjects with previous

neuromusculoskeletal spine trauma, systemic rheumatological condition, who had undergone major abdominal, lung or spinal surgery, or who had a recent infection treated with antibiotics were excluded.

The sample size (n≥64; 32 in each group) was calculated based on a previous study (Heneghan *et al.,* 2009) and was based on being able to detect a minimum clinically important difference (10 degrees) in thoracic spinal axial rotation movements between the two groups, based on power of 0.8, and at the 5% significance level (Brant, 2010). In order to reduce the variance of measures in the control group recruitment in this group was not limited to thirty two.

5.2.4. Procedure and measurement instruments

A pilot study was undertaken to determine the feasibility of the protocol (See appendix 9), with a number of minor changes being subsequently made. These included removal of the COPD Self efficacy questionnaire, and omission of muscle length and grip strength testing due to time constraints and patient fatigue.

During a single visit, participants were screened to confirm they met the inclusion criteria, completed a written consent and underwent an assessment by the author, an experienced musculoskeletal physiotherapist. Data collection was taken between the hours of 10.00 and 4.00 to minimise the diurnal variation of measures with environmental factors, such as temperature remaining consistent throughout the duration of testing.

The main exposure measure was assessment of lung function, and the performance-based outcome measures or predictors included posture (cervical and thoracic), spinal mobility (cervical lateral flexion, and cervical and thoracic axial rotation) and muscle sensitivity (Pectoralis minor, sternocleidomastoid, anterior scalene and upper trapezius) details of which are provided below and summarised in table 10.

Lung Function

A hand-held Micro Spirometer, (CareFusion, UK) was used to measure FVC, FEV_1, where FVC, is the amount of air forcibly exhaled after taking a maximum inhalation and FEV_1, forced expiratory volume in one second, is the amount of air which can be forcibly exhaled in the first second. This data was used to calculate FEV_1/FVC which provides a measure of the ratio of FEV_1 to FVC expressed as a fraction (GOLD, 2010). FEV_1 is a highly reproducible measure of airflow obstruction, used extensively as an outcome measure of clinical trials of COPD and used as the preferred measure for diagnosing disease severity (Wise, 2006). In accordance to clinical guidelines the ratio of FEV_1/FVC is used to define presence or absence of airflow obstruction (Wise, 2006; GOLD, 2011).

Posture

Postural changes are often reported in COPD (Chaitow, 2002) yet there remain no known studies that have measured cervico-thoracic posture in COPD. As discussed in section 1.3.2. a forward head posture is often adopted to open the upper airways (Courtney, 2009). Whilst secondary or beneficial for ventilation in the short term, these musculoskeletal adaptations may lead to altered biomechanics and or musculoskeletal pathologies and pain (Courtney, 2009). A recent study among patients with asthma reported statistically significant differences in cervico-thoracic posture between a sample of subjects with asthma (n=30) compared to controls. Forward head posture was 8-degrees (95% confidence interval 0.0, 12.7) in the mild persistent asthma group, 11-degrees (95% confidence interval 0.0-20.50 in the severe persistent asthma group and 6-degrees (1.3, 28.7) in the control group (Lunardi *et al.,* 2010). Additionally 50% of the asthma group experienced chronic pain in the region of the neck, shoulder and thoracolumbar regions indicative of musculoskeletal dysfunction. The control group in contrast reported no symptoms (Lunardi *et al.,* 2010).

Using a widely adopted approach (Raine *et al.,* 1997; Katzman *et al.,* 2007; Silva *et al.,* 2010) postural angles were measured. Postural angles were measured for the upper thoracic region, upper and lower cervical regions using a digital image processing program developed by the National Institutes of Health, USA (Collins, 2007). Whilst many studies have utilised this approach for cervical spine measures (Raine *et al.,* 1997; Niekerk *et al.,* 2008; Silva *et al.,* 2010), this non-invasive approach was adapted for thoracic postural measurement. Other research measuring thoracic posture has included use of 'flexicurve' (Hinman, 2004) or, more recently, gravity dependant inclinometers (Lewis and Valentine, 2010; Johnson *et al.,* 2012). However, to minimise the number of testing positions used and to ensure standardisation of procedure for all participants, a seated position was deemed most appropriate for the evaluation of thoracic spine posture for this population.

Spinal mobility

There are no published studies that have specifically investigated changes to joint mobility (cervical and thoracic spinal range of motion) in COPD patients. Rib cage stiffness is often reported in COPD (Miller, 1975; Masarsky & Weber, 1988; Noll *et al.,* 2009) and likely a consequence of changes in the musculoskeletal system described in section 1.3.3., and 1.4. Quantifying stiffness in such a complex body region is challenging, therefore a measure of range of motion offered a viable alternative. The rationale for using thoracic axial rotation was based on coupling between thoracic vertebrae and ribs described in section 1.3.3. This was also due to a lack of confidence in the existing and published measures using skin sensors over the chest wall (Culham et al., 1994; Leong *et al.,* 1999) or surface measures using a tape measure (Putt *et al.,* 2008; Leelarungrayub *et al.,* 2009; Malaguti *et al.,* 2009) (section 3.3). Motion analysis (Polhemus, Liberty ™) in combination with ultrasound imaging of first thoracic vertebrae was therefore used to assess thoracic axial rotation (Heneghan *et al.,* 2009). Notwithstanding the use of different populations motion analysis for spinal range of motion has been shown to be stable

and reliable for intra-tester measures of thoracic spine rotation in a population of young adults, ICC $_{(2,1)}$ 0.89-0.98 (Heneghan *et al.,* 2009).

Measuring cervical rotation and lateral flexion would potentially provide information on the influence of muscles which act both on the rib cage as accessory muscles of respiration and contribute to cervical spine motion, namely sternocleidomastoid, scalenes and upper trapezius (section 1.4). Furthermore cervical range of motion is, as has been previously investigated, related to postural changes (Yoo & An, 2009). For the cervical spine, measures were recorded using a single electrode mounted on a pair of safety glasses as has been done and documented previously (Jordan *et al.,* 2000). Intra-tester reliability of motion analysis of cervical rotation, using the same methodology was found to be ICC $_{(2,1)}$ 0.79 p=0.79 in a healthy subjects (Jordan *et al.,* 2000).

Muscle sensitivity

Skeletal muscles have been shown to become sensitised in the presence of inflammation linked to the development of trigger points (Shah *et al*., 2005). As well as a possible cause of musculoskeletal symptoms, research has shown that trigger points in skeletal muscles adversely influence muscle activation (Lucas *et al.,* 2010). Although studies have previously investigated activity levels in accessory muscles of respiration in COPD (De Troyer *et al.,* 1994; Gandevia *et al.,* 1996; Peche et al., 1996; de Andrade *et al.,* 2005; Putt *et al.,* 2008; Duiverman *et al.,* 2009) little attention has been given to musculoskeletal symptoms. Increased accessory respiratory muscle activity associated with dyspnoea and chest wall stiffness may contribute to the development of trigger points or sensitised muscles in the cervico-thoracic region (Estenne *et al.,* 1998). Sensitivity of known trigger points in cervico-thoracic muscles was therefore measured using a hand-held pressure algometer (Somedic Production AB, Sweden). This is a technique used widely in musculoskeletal research but is now becoming recognised as a useful means of quantifying muscle sensitivity in other presentations (Johansson *et al.,* 2012).

Selection of muscles for the current study was based on empirical evidence of mapped trigger points (Travell & Simons, 1983) and their role as accessory muscles of respiration and association with cervico-thoracic posture. Test-retest reliability of pressure algometry has been shown to be satisfactory to good (ICC 0.78–0.93) for neck muscles of healthy subjects (Ylinen *et al.,* 2007).

Additional measures

In addition, a number of socio-demographic and other health measures which were potential confounders were assessed through patient report using questionnaires and performance-based measures from physical examination. All measures are outlined in more detail below, and summarised in Table 10.

Table 10. Exposure and predictor variables

	Measure and measurement properties	COPD	Control	Instrument
Pulmonary function	**FEV_1** (percent predicted) Responsive physiologic measure of airflow and widely used in research/clinical practice to define severity of the disease (Wise, 2006) I. Mild COPD: FEV_1 >/= 80% predicted, FEV_1/FVC < 0.7 II. Moderate COPD: 50% </= FEV_1 < 80% predicted, FEV_1/FVC < 0.7 III. Severe COPD: 30% </= FEV_1 < 50% predicted, FEV_1/FVC < 0.7 (GOLD 2011)	√	√	Hand-held Spirometer (Micro Spirometer, CareFusion, UK)
	FVC (percent predicted)	√	√	
	FEV_1/FVC ratio Used to define presence or absence of airflow (Wise, 2006)	√	√	
Spinal range of motion	**Cervical lateral flexion** (degrees) A reliable measure of cervical rotation (inter-observer ICC $_{2,1}$ 0.81 p>0.70) . Values derived from sample of n=40 age 33.7±9.21; 90.9±14.42-degrees, 95% CI 87.5, 94.3) (Jordan *et al*., 2000)	√	√	Polhemus (Liberty™) motion analysis system (Colchester, Vermont, USA)
	Cervical axial rotation (degrees) A reliable measure of cervical rotation (inter-observer ICC $_{2,1}$ 0.85 p>0.76) . Values derived from sample of n=40 age 33.7±9.21; 158.5±15.52-degrees, 95% CI 154.7, 162.0) (Jordan *et al*., 2000)	√	√	Polhemus (Liberty™) motion analysis system (Colchester, Vermont, USA)
	Thoracic axial rotation (degrees) A reliable measure of thoracic rotation (within day intra-observer ICC $_{2,1}$ 0.89-0.98) Values derived from sample of n=24 age 24.96±2.6; 85.15-degrees) (Heneghan *et al,* 2009)	√	√	Polhemus (Liberty™) motion analysis system (Colchester, Vermont, USA)
Posture	**Cervical posture**: Tragus-forehead line and vertical axis(degrees) Reliable and valid measure of evaluating sitting posture of the upper-body as measured against radiographic images (Niekerk *et al.,* 2008)	√	√	Digital images imported to a PC and analysed using an online system (National

	Measure and measurement properties	COPD	Control	Instrument
	Cervical posture: Tragus-C7 and vertical axis angle(degrees) (Raine *et al*., 1997) Reliable and valid measure of evaluating sitting posture of the upper-body as measured against radiographic images (Niekerk et al., 2008)	√	√	Institutes of Health. USA (Collins, 2007)
	Thoracic posture: T8-C7 and vertical axis angle (degrees)	√	√	
Muscle tenderness (bilateral)	**Pectoralis minor** (kPa) Reference values not known	√	√	Pressure algometry
	Sternocleidomastoid (kPa) Reference values not known	√	√	
	Anterior scalene (kPa) Reference values not known	√	√	
	Upper trapezius (kPa) Reference values not known	√	√	
Bone mineral density	**Bone mineral density** (g/cm²) Normal: 1000 to 1200 g/cm² T-scores • Normal:-1.0 or higher • Osteopenia:-1.0 to -2.5 • Osteoporosis:-2.5 or lower (WHO, 2003)	√	√	Bone mineral density and T score DXA Whole Body Scanner, Hologic, Discovery QDR
Sociodemographic data	**Age (years)**	√	√	Screening tool
	Smoking history (pack years)	√	√	
	Occupational history	√	√	
	Musculoskeletal past medical history	√	√	
	Drug history to include steroid use	√	√	
	Oxygen use (hours / day)	√		
	Weight (Kg)	√	√	
	Height (m)	√	√	
Dyspnoea	**MRC Dyspnoea scale** Scale 1-5 A simple and valid measure tool which can categorise patients in terms of their disability (Bestall *et al.,* 1999) 1. Not troubled by breathlessness except on strenuous exercise 2. 2: Short of breath when hurrying or walking up a slight hill 3. 3: Walks slower than contemporaries on level ground because of breathlessness, or has to stop for breath when walking at own pace 4. 4: Stops for breath after walking about 100m or after a few minutes on level ground 5. 5: Too breathless to leave the house, or breathless when	√	√	MRC Dyspnoea scale

	Measure and measurement properties	COPD	Control	Instrument
	dressing or undressing (Fletcher *et al.,* 1959; Bestall *et al.,* 1999)			
Health related quality of life	**St Georges Respiratory Questionnaire** A valid disease-specific measure weighted to produce three component scores from 76 items; symptoms, activity, and impact. A total score provides a global measure of respiratory health. Scores range from 0% to 100% with 100 indicating maximum disability (Jones *et al.,* 1991; Weldam *et al*., 2013)	√		St George's Respiratory Questionnaire
Anxiety and depression	**Hospital Anxiety and Depression Scale** 14 question (7 relating to anxiety and 7 to depression). Self report format and graded according to relative frequency of symptoms during previous week. Responses scored, summed with each ranging 0-21 for each scale. Anxiety & Depression. • Normal: 0-7 • Borderline abnormal: 8-10 • Abnormal:11-21 Valid and reliable in non-psychiatric populations (Zigmond & Snaith, 1983	√	√	Hospital Anxiety and Depression Scale (approval to use gained)
Functional limitation due to spinal pain	**Neck Disability Index** A valid, reliable and responsive self-complete tool to detect disability associated with neck pain of a range of causes. There are 10 questions which are scored out of 50 and a percentage calculated. Reliability coefficient ICC 0.50-0.98. Test-retest reliability 0.73-0.99. MCID reported to be between 5 -10 points. The clinically important difference is reported to be 5-19 points. • No disability: 0-8% • Mild disability: 10-28%. • Moderate 30-48% • Severe: 50-68% • Complete: 70% or more (Vernon & Mior, 1991; Macdermid *et al.,* 2009)	√	√	Neck Disability Index
	Oswestry Disability Index A valid, reliable and responsive self-complete tool to detect disability associated with low back pain. There are 10 questions which are ranked and an overall score derived and percentage calculated. Internal consistency range from 0.71-0.87 and test-retest reliability r=0.83 to 0.99. MCID reported to be between 4 and	√	√	Oswestry Back Disability Index

	Measure and measurement properties	COPD	Control	Instrument
	10.5 points. • Minimal disability: 0- 20% • Moderate disability:21-40% • Severe disability:41-60% • Crippled:61-80% • Complete: 81-100% (Fairbank & Pynsent, 2000; Vianin 2008)			
Current neck pain	**Numerical Rating Scale-Neck** 0-10 scale Test-retest reliability ICC=0.76; 95% CI, 0.51,0.87). MCID 1.3 for the NRS in subjects with mechanical neck pain. • No pain : 0 • Mild pain: 1-3 • Moderate pain: 4-6 • Severe pain: 7-10 (Williamson *et al*., 2005; Cleland *et al.,* 2008)	√	√	Visual analogue scale
Current back pain	**Numerical Rating Scale-Back** Self-reported rating of symptom bothersomeness • No pain : 0 • Mild pain: 1-3 • Moderate pain: 4-6 • Severe pain: 7-10 (Williamson *et al*., 2005)	√	√	
Oxygen saturation	Percent	√	√	Pulse oximeter

5.3. Exposure

Pulmonary function; measured in accordance to the British Thoracic Society (BTS)/ Association for Respiratory Technology and Physiology (ARTP) Guidelines (1994). Three measures of FEV_1 and FVC were taken, with the highest result from each being used for the analysis. The difference between the best and worst performance were required to be less than 5% (BTS COPD Consortium, 2005) with repeated measures being taken as necessary up to a maximum of five efforts. Percent predicted values for each participant of normal values were subsequently calculated using the reference equations from BTS COPD Consortium (BTS COPD Consortium, 2005). For the purpose of this study, COPD was defined as a participant having FEV_1/FVC ratio

of <70% (GOLD, 2010). Classification of severity of disease, mild, moderate or severe was based on GOLD criteria I, II or III respectively.

5.4. Predictors

Spinal range of motion (ROM); full active thoracic axial rotation and cervical axial rotation and lateral flexion, were measured using motion analysis (Polhemus, Liberty™).

Participants, as in previous thoracic spine motion analysis studies (Willems *et al.,* 1996; Edmondston *et al.,* 2007) were instructed to sit upright with their lumbar spine in a neutral position (mid-point between full lumbar flexion and extension). Their legs were fully supported throughout the procedure with their hips and knees positioned at 90-degree angle with a seatbelt across their thighs to limit movement to the spine during rotation. Shoulders were stabilised manually to limit cervical motion to the cervical spine and foot switch used to capture data on a computer using the Polhemus, Liberty™ software. For thoracic rotation participants were asked to place hands across chest and rotate fully to the right and left, holding the position at the end of range until an image of the C7 vertebra, with laminae clearly visible, had been acquired and position of the transducer captured using the Polhemus, Liberty™ software (Willems *et al.,* 1996; Heneghan *et al.,* 2010).

Spinal posture; as there are no studies that have evaluated spinal postural angles in COPD, static sitting spinal posture was measured. Digital photographs (Figure 16) in the sagittal plane were taken in a standardised up right sitting position, with feet supported, knees and hips at 90-degree angle, lumbar spine in neutral position. Self-adhesive markers (yellow) were attached to the skin overlying the C7, T8 spinous processes. From on screen images postural angles were measured the position of the markers and anatomical reference points for lateral eye crease and tragus (Figure 14):

1) Angle between tragus-lateral eye and vertical axis indicates the position of the head relative to the neck and an increase in this angle is indicative of a forward-chin posture (Nierkerk *et al*., 2008) (green)

2) Angle between tragus-C7 and vertical axis is a measure of forward-head position and a marker of mid-lower cervical spine posture with increased angulation being associated with increased activity of superficial neck flexor muscles, such as sternocleidomastoid muscle (Nierkerk *et al.,* 2008) (red)

3) Angle between T8-C7 and vertical axis is a measure of upper thoracic kyphosis and may be indicative of changes in thoracic vertebral bone morphology secondary to changes in bone mineral density or postural changes associated with dyspnoea (Raine *et al.,* 1997; Katzman *et al.,* 2007; Silva *et al.,* 2010) (yellow).

Each angle was measured on line three times and the derived mean measure used for data analysis.

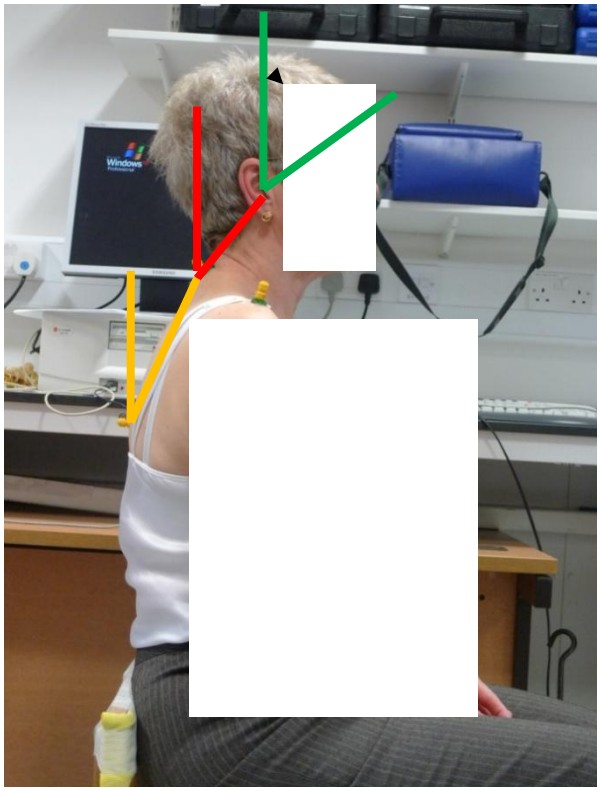
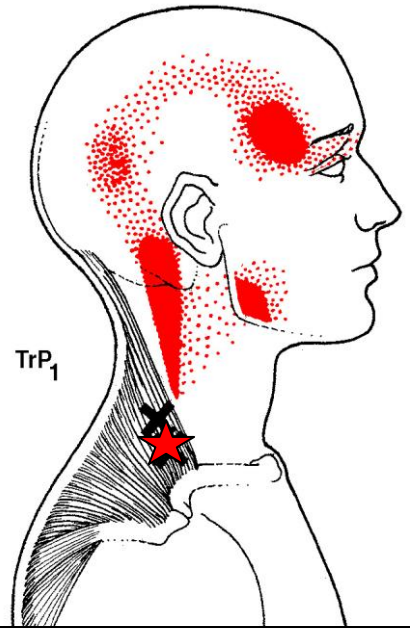
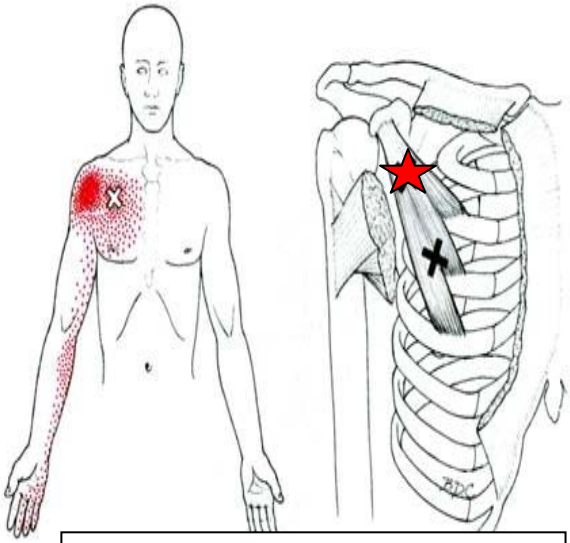


Figure 14. Experimental set up for digital image illustrating position of skin markers at T8 and C7

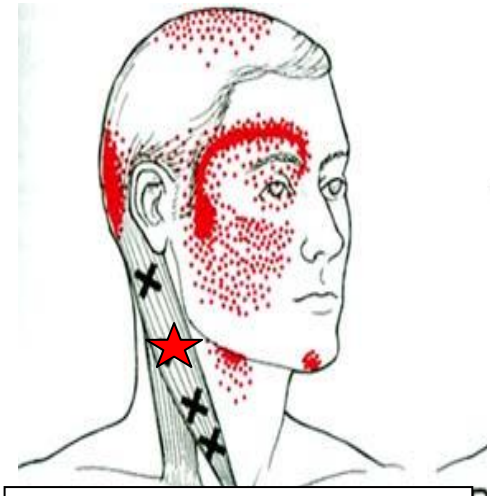
Muscle tenderness; Pressure pain thresholds for known trigger point sites were evaluated for the following muscles: pectoralis minor, upper trapezius (TrP1), sternocleidomastoid, anterior scalene, bilaterally using a pressure application rate of 40kPa/s (Travell & Simons, 1983) (see Figure 15). Where more than one trigger point existed within a muscle (sternocleidomastoid, pectoralis minor and trapezius) selection was based on the researcher's expertise linked to ability to identify the same point on different subjects using anatomical landmarks with consistency. Familiarisation of the procedure using a lower arm muscle preceded testing with participants being asked to advise the researcher of the exact point at which the sensation of pressure was beginning to feel uncomfortable. This corresponds with the pressure pain threshold widely reported in other studies (Shah *et al.,* 2008; Johansson *et al.,* 2012).



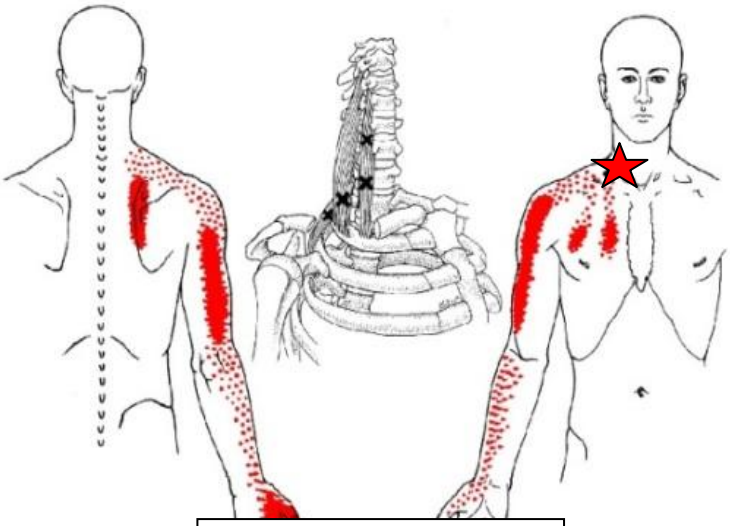
a. Upper trapezius trigger point (TrP 1)



b. Pectoralis minor trigger point



c. Sternocleidomastoid trigger point



d. Scalene trigger point

Figure 15. Trigger point sites of a: Upper Trapezius, b: Pectoralis Minor, c: Sternocleidomastoid, and d: Anterior Scalene (Travell & Simons, 1993); ★; denotes trigger point used.

5.5. Confounding variables

Many factors have been shown to influence COPD exacerbation rates or severity, as a result may need to be adjusted for within the analysis.

- Anxiety and depression were measured using the Hospital Anxiety and Depression Score (HADS) (Appendix 10) (Zigmond & Snaith, 1983; Cheung *et al*., 2011).
- Details of age (years), smoking history to calculate pack years (number of cigarettes smoked per day, divided by 20, multiplied by the number of years smoked) (Boehringer-Ingelheim & Pfizer, 2010) were obtained through a self-completed questionnaire.
- Body mass index was calculated using measures of height (metres) and weight (Kg) taken on the day of testing. Measurement of height was made by clinical stadiometer with shoes removed. Body weight was measured with a calibrated scale with participants wearing clothes but without shoes.

5.6. Patient reported outcome measures

5.6.1. COPD group

For patients with a COPD diagnosis, a disease specific health related quality of life questionnaire, the St George's Respiratory Questionnaire (SGRQ) (Jones *et al.,* 1992), was administered. This questionnaire consists of fifty items, subset scales for symptoms, activity and impact and provides a total score for health-related quality of life. Component and total scores range from 0-100%, with 0% indicating no impact on health-related quality of life (Jones *et al.,* 1991).

5.6.2. COPD and Control group

The Medical Research Council (MRC) dyspnoea scale (Stenton, 2008) (Appendix 11) was used to evaluate breathlessness in the whole sample. As COPD diagnosis was based on clinical diagnosis

(GP or consultant), breathlessness was assessed to assist identification of undiagnosed respiratory disease or dysfunction. The MRC dyspnoea scale has also been validated as a measure of disability in COPD (Bestall *et al*., 1999). Anxiety and depression were measured using the Hospital Anxiety and Depression Score (HADS) (Appendix 10) (Zigmond & Snaith, 1983; Cheung *et al*., 2011). This has been widely used in COPD research as a discrete measure of psychological status (Cheung *et al*., 2011).

Functional impairment due to back or neck pain was measured using the Neck Disability Index (NDI) (Appendix 12) (Vernon & Mior, 1991) and Oswestry Disability Index (ODI) (Appendix 13) (Fairbank & Pynsent, 2000) respectively. Both measures are widely used in spinal research, as they are simple to complete and provide an indication of disability for spinal pain of musculoskeletal origin. The questionnaires comprise of 10-item questionnaires, which measure the impact of symptoms on activities of daily living. Both scales are calculated as percentage disability and reference values are provided in Table 13.

In order to assess current discomfort arising from neck or back, a numerical rating scale (NRS) (rating 1-10) was used and participants were asked to rate the extent to which current neck (NRS-N) or back symptoms (NRS-B) bothered them. With the sample being older adults, it is reasonable to consider that many participants may have mild symptoms (aches and pains) of musculoskeletal origin; indicative of musculoskeletal tissue stress, but at a level that would not necessarily warrant formal clinical or medical management. Participants with a history of significant spinal pathology were, however, excluded. NRS have been reported as valid, reliable and appropriate measurement tool for use in clinical practice (Williamson *et al*., 2005).

5.6.3. Other measures

Bone mineral density (BMD); Dual-emission X-ray absorptiometry (DXA) (DXA Whole Body Scanner, Hologic, Discovery QDR) was used to determine full body BMD expressed as g/cm^2, and

T-scores. T-score provides a standardised score for BMD, as it compares a subject's BMD to that of a healthy thirty-year-old of the same sex and ethnicity, allowing comparison between participants (WHO, 2003). Where participants had undergone a DEXA scan in the last year, results were requested from their GP. A fully trained research assistant undertook all scanning and analysis of results.

Resting arterial saturation was measured using a pulse oximeter (GE Datex Ohmeda 3900P, Pulse Oximeter). This was used as a reference value, but also to monitor for exercise induced hypoxia throughout data collection. Details of past and current medication use, including courses of oral steroid use, occupational background, past musculoskeletal medical history was also recorded (Appendix 14). BMI was calculated from raw values for height and weight recorded on the day of testing (NHLBI, 2010).

5.6.4. Bias

A number of measures were put in place to minimise the influence of bias. All measures were taken by one researcher and in accordance with recognised guidelines where available, such as BTS/ARTP Guidelines for spirometry (1994). Familiarisation and piloting the testing procedure was conducted prior to the start of the main study.

5.6.5. Ethics

Ethical approval was granted by the National Research Ethics Service, South Birmingham (Ref number: 09/H1207/122). Adherence to Institutional Research Governance was maintained throughout. See appendix 15.

5.6.6. Data analysis

Descriptive analysis was used to compare musculoskeletal outcomes for the COPD group and matched controls using means and standard deviations. Differences between COPD and control

participants were evaluated using independent sample t-tests based on the data being normally distributed. Error bars of mean values and 95% confidence intervals are included to display differences for main performance-based musculoskeletal outcomes.

Scatter graphs were reviewed to determine that a linear relationship existed. The strength of association between performance-based measures of pulmonary function and other predictor outcomes variables was evaluated using Pearson Product-moment correlation coefficient where data was shown to be normally distributed (Kolmogorov-Sminov test of normality) for the two samples across continuous variables. Spearman's rank order correlation coefficient was used as a non-parametric alternative when data was not normally distributed. Strength of associations were determined based on established criteria (Pett, 1997): values between 0.00 and 0.25 indicate weak or no association; values between 0.26 and 0.50 indicate a low degree of association; values between 0.51 and 0.75 indicate a moderate to strong degree of association and values between 0.76 and 1.00 indicate a very strong degree of association. However given the likely and possible influences of confounders on the results limiting data analysis to simple bivariate correlations was unacceptable.

Having checked the data for necessary prerequisites, hierarchical multiple linear regression modelling was performed to further examine the relationship between severity of airway obstruction (FEV_1) and musculoskeletal performance-based measures across the total sample. This was done separately for each measure as the sample size precluded all independent variables being included together in one model (Stevens, 1996, p.72). Three models were subsequently used for each measure to enable progressive adjustment for known confounding variables: Model 1 (minimally adjusted model) adjusted for age, BMI and sex; Model 2 additionally adjusted for anxiety and depression using HADS (Maurer *et al.,* 2008); and Model 3 with additional adjustment for smoking history (Forey *et al.,* 2011).

Secondarily logistic regression analysis was performed to evaluate the presence and strength of association between COPD and musculoskeletal changes. As with the linear regression modelling, three models were used; one with minimal adjustment using age, BMI and sex, along with 2 further models, to adjust for HADS and smoking. All data analysis was performed using SPSS version 18.00. Missing data was generally dealt with using mean substitution. However regression substitution was considered as a more robust approach in cases where many data points were missing and the sample size adversely affected. Probability values of <0.05 were considered significant.

The main analysis was based on classifying participants to COPD or normal according to physician diagnosis. A sensitivity analysis was also undertaken to repeat analyses according to a spirometry definition of COPD, based on the GOLD criteria (GOLD, 2011).

5.7. Results

The COPD sample, based on referring diagnosis included participants with mild (GOLD stage I) (n=12), moderate (GOLD stage II) (n=13) and severe (GOLD stage III) (n=6) COPD and no definable airflow obstruction (n=2) (GOLD, 2011), and the control group of 55 participants. For flow of participants through the study including withdrawals and reason for withdrawal see table 11

Table 11: Recruitment details and attrition

	Contacts made	Met inclusion /exclusion criteria (n=)	Reason for exclusion	Final numbers (n=)	Reason for withdrawal
Breathe Easy Support Group	N=18 COPD n=16 Control n=2	N=12 COPD n=10 Control n=2	Pacemaker n=1 Anticoagulation medication n=1 Chest infection n=2	N=8 COPD n=6 Control n=2	Chest infection n=2 Family bereavement n=1 No longer wished to participate n=1
Regional Pulmonary Rehabilitation Groups	N= 25 COPD n=21 Control n=4	N=18 COPD n=14 Control n=4	Anticoagulation medication n=1 Chest/abdominal surgery n=4 Chest infection n=1 Spinal problems n=1	N=18 COPD n=14 Control n=4	
Birmingham Elders Database and University personnel	N=22 COPD n=2 Control n=20	N=20 COPD n=1 Control n=19	No longer wished to participate n=1 On holiday n=1	N=20 COPD n=1 Control n=19	
Respiratory Outpatient Department	N=14 COPD n=14 Control n=0	N=10 COPD n=10 Control n=0	Chest/abdominal surgery n=1 Chest infection n=1 Spinal problems n=1 No longer wished to participate n=1	N=10 COPD n=10 Control n=0	
Word of mouth	N=33 COPD n=2 Control n=31	N=32 COPD n=2 Control n=30	Chest/abdominal surgery n=1	N=32 COPD n=2 Control n=30	
Total sample	112	92		88	

5.7.1. Descriptive results and comparison of groups

The characteristics of participants included in the study is summarised in Table 12. The groups were comparable with respect to age, sex and BMI, although smoking (mean pack years) and steroid use were considerably higher for the COPD group ($p<0.001$).

COPD Group. SGRQ scores for symptoms, activity and impact were 72.86% (19.53), 77.11% (4.32), 46.61% (3.73) respectively, with a combined total score for SGRQ of 60.28% (3.51), and indicative that COPD had a significant impact on their health-related quality of life. Just over half of the COPD participants had previously attended pulmonary rehabilitation (n=24), with eight participants on oxygen for an average of 12.25 hours per day.

Table 12. Descriptive characteristics of COPD and matched controls.

Characteristic	Control	COPD	p-value (95% CI)
	N=55	N=33	
Mean age (years)	66.58 (5.95)	67.22(8.52)	0.81 (-2.96, 3.80)
Sex F/M	37/18 67% F, 33% M	18/15 55% F, 45% M	
Mean BMI *Height* *Weight*	26.56 (4.47) *165.44 (9.22)* *73.42 (16.52)*	26.85 (5.40) *165.64 (8.28)* *74.09 (17.67)*	0.79 (-1.83, 2.41) *0.96 (-3.80, 3.98)* *0.86 (-6.75, 8.10)*
Smoking history (Mean pack years)	7.70 (13.05)	53.18 (36.08)	<0.001 (32.26, 58.69)**
Steroid use (average courses/year)	0.03 (0.14)	2.86 (3.19)	<0.001 (1.70, 3.96)**
Spirometry			
Mean FEV_1 (% predicted)	104.53 (16.86)	50.94 (19.40)	<0.001 (-61.40, -45.78)**
Mean FVC (% predicted)	114.51 (20.42)	92.06 (23.09)	<0.001(-31.84, -13.06)**
Mean FEV_1/FVC	0.76 (0.10)	0.45 (0.12)	<0.001(-0.36, -0.27)**
Oxygen saturation (%)	94.68 (0.92)	92.31 (3.39)	<0.001(-3.61, -1.12)**
Medical Research Council Dyspnoea scale • Grade 1 • Grade 2 • Grade 3	 54 (98.2%) 1 (0.2%) 0	 0 10 (30.3%) 3 (9.1%)	 <0.001(2.97, 3.69)**

Characteristic	Control	COPD	p-value (95% CI)
• Grade 4 • Grade 5	0 0	18 (54.5%) 2 (6.1%)	
Joint (degrees)			
Cervical spine rotation	124.30 (24.69)	109.85 (26.56)	0.01 (-25.57, -3.33)*
Cervical spine lateral flexion	79.44 (24.67)	76.71 (22.39)	0.61 (-13.32, 7.85)
Thoracic spine rotation	54.01 (15.67)	38.77 (12.59)	<0.001 (-21.64, -8.86)**
Posture (degrees)			
T8-C7 to vertical	25.72 (4.99)	27.01 (6.00)	0.30 (-1.17, 3.74)
C7-tragus to vertical	45.99 (6.37)	49.22 (10.05)	0.12 (-0.88, 7.33)
Tragus-eye to vertical	72.73 (7.60)	73.40 (8.51)	0.72 (-2.96, 4.29)
Muscle pressure pain threshold (PPT) (kPa)			
Right Pectoralis minor	197.10 (96.30)	156.45 (83.43)	0.06 (-83.06, 1.77)
Right trapezius	234.22 (110.88)	186.93 (97.66)	0.06 (-96.07, 1.49)
Right Sternocleidomastoid	103.48 (49.86)	78.97 (35.98)	0.02 (-45.38, -3.66)*
Right Scalene	117.08 (57.23)	90.34 (42.93)	0.03 (-50.94, -2.52)*
Left Pectoralis minor	197.60 (90.10)	154.76 (71.83)	0.03 (-81.53, -4.16)*
Left trapezius	228.92 (101.601)	184.38 (92.49)	0.05 (-89.83, 0.74)
Left	105.91 (49.94)	85.34 (40.66)	0.06 (-41.75, 0.62)

Characteristic	Control	COPD	p-value (95% CI)
Sternocleidomastoid			
Left Scalene	117.30 (50.16)	99.86 (54.52)	0.15 (-41.12, 6.25)
Total pressure pain threshold	1260.89 (588.48)	911.33 (555.05)	0.01 (-601.81,-97.31) *
Bone			
Bone mineral density (gr/cm2)	1.07 (0.12)	1.02 (0.11)	0.09 (-0.99, 0.01)
T score	-0.69 (1.19)	-1.26 (1.13) Osteopoenic	0.04 (-1.09, -0.04) *
Questionnaires			
Hospital Anxiety and Depression Scale	7.71(4.83)	14.52 (6.82)	<0.001 (4.09, 9.52)**
Neck Disability Index (%)	7.56 (8.80)	12.12 (15.24) Mild disability	0.12 (-1.30, 10.41)
Oswestry Disability Index (%)	9.82 (10.87)	10.48 (13.43) Minimal disability	0.80 (-4.54, 5.87)
Numerical rating scale-neck Percentage of subjects reporting bothersomeness (VAS≥1)	1.63 (2.17) 54%	2.45 (2.41) 70%	0.10 (-0.17, 1.82)
Numerical rating scale-back Percentage of subjects reporting bothersomeness (VAS≥1)	1.96 (2.19) 59%	2.79 (2.71) 64%	0.15 (-0.29, 1.94)

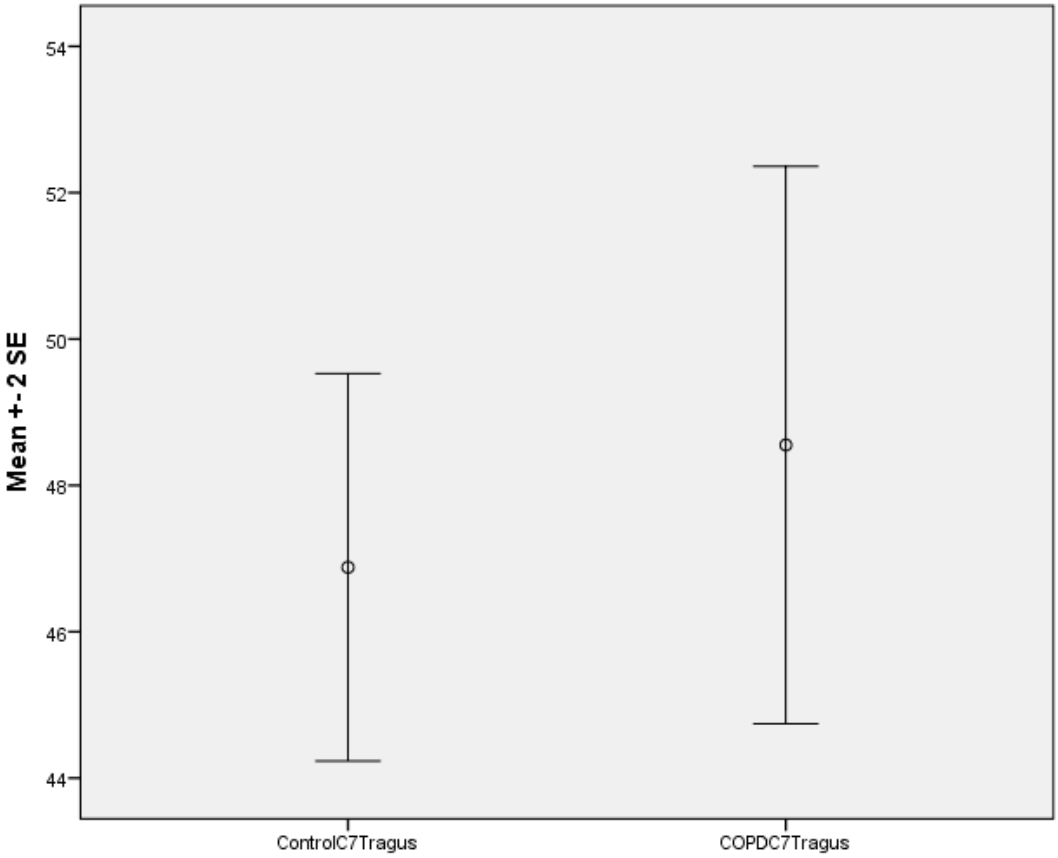
5.8. Respiratory measures

There were statistically significant differences in spirometry and oxygen saturation between the COPD and control groups, reflective of the diagnostic clinical features of COPD. Dyspnoea scores also differed considerably, with the majority of participants in the COPD group rated as dyspnoea Grade 4, 'stops for breath after walking 100 yards or after a few minutes on level ground', compared to most of the control population being grade 1 (Stenton, 2008).

5.8.1. Musculoskeletal measures

Postural measures

Postural measures were similar across groups, although the C7-tragus to vertical measure was higher for the COPD group (Figure 16). Whilst the difference between groups for C7-tragus was not statistically significant, this finding is consistent with increased accessory muscle activity in COPD and adaptation to facilitate opening of upper airways (de Andrade *et al.,* 2005; Courtney, 2009).

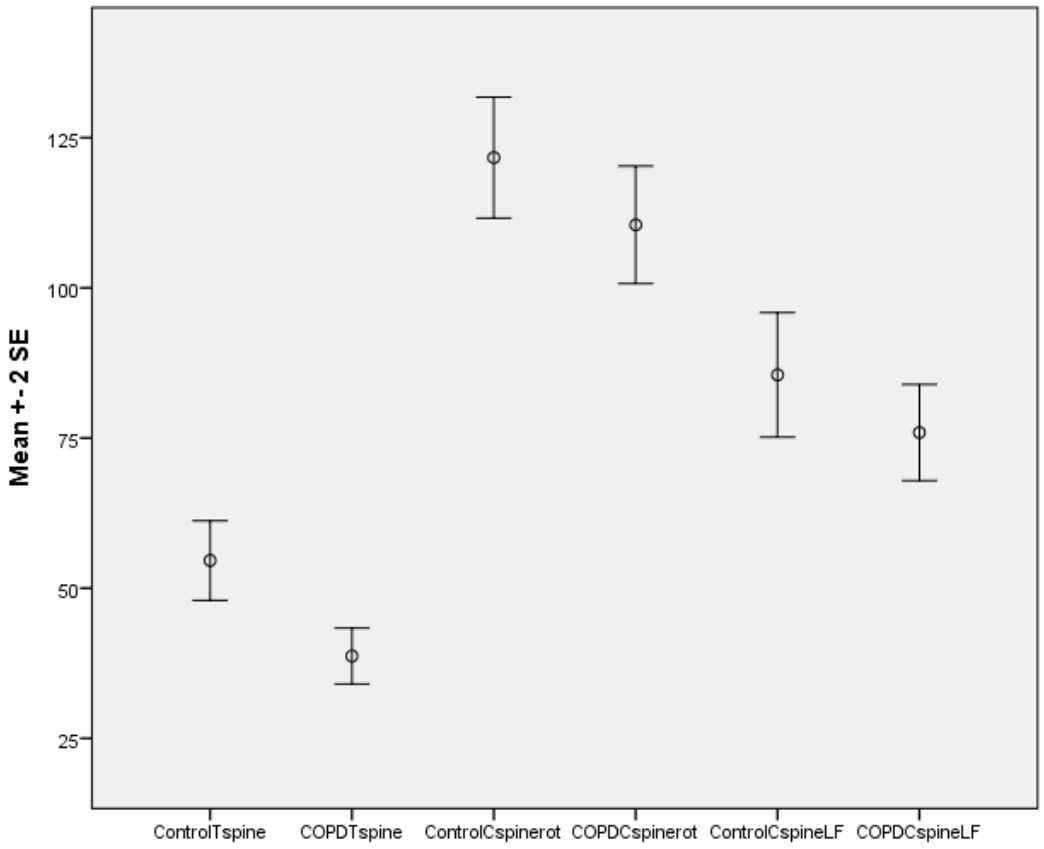


ControlC7Tragus; Control group C7-tragus angle (n=55), *COPDC7Tragus; COPD group C7-tragus angle* (n=33)

Figure 16. Comparison of cervical posture between COPD and control participants for C7-tragus measure.

Spinal Range of Motion

Spinal ranges of motion differed between groups, with the COPD group exhibiting a reduction in active cervical lateral flexion, rotation and thoracic rotation compared to the control group, with statistically significant differences being achieved for cervical rotation and thoracic rotation 109.85 (26.56), 38.77 (12.59) degrees respectively compared to 124.30 (24.69) and 54.01(15.67) degrees respectively in the control group (see Figure 17).

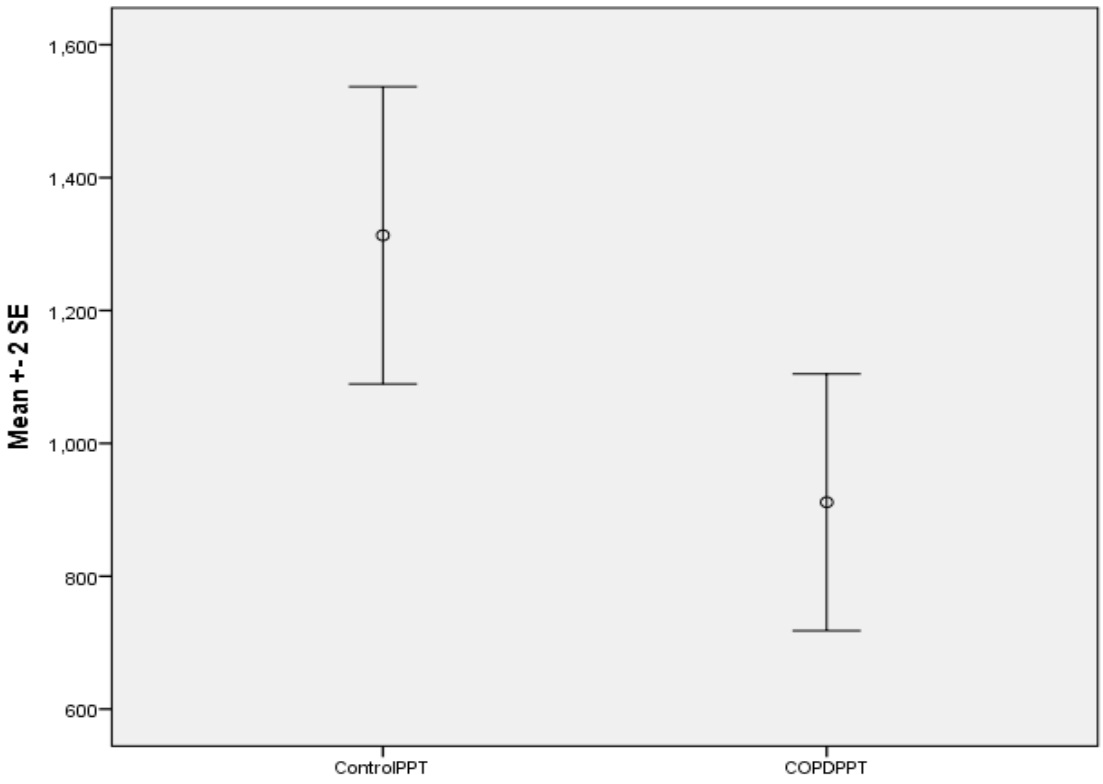


ControlTspine; control group thoracic spine rotation, COPDTspine; COPD group thoracic spine rotation, ControlCspinerot; control group cervical spine rotation, COPDCspinerot; COPD group cervical spine rotation, ControlCspineLF; Control group cervical lateral flexion (n=52), COPDCspineLF; COPD group cervical lateral flexion (n=32)

Figure 17. Comparison spinal motion between COPD and control subjects for thoracic axial rotation, cervical axial rotation and lateral flexion.

Pressure pain threshold

Differences in pressure pain thresholds were noted for all muscles between groups, with the COPD group generally having lower pain thresholds, or being more sensitive However, whilst a number of individual muscle measures were statistically significant, right sternocleidomastoid (p=0.02), right scalene (p=0.03), left pectoralis minor (p=0.03) no consistent pattern was seen overall. Total pooled PPT scores did however indicate that participants with COPD have statistically significantly lower pressure pain thresholds compared to controls (p=0.01). See Figure 18.

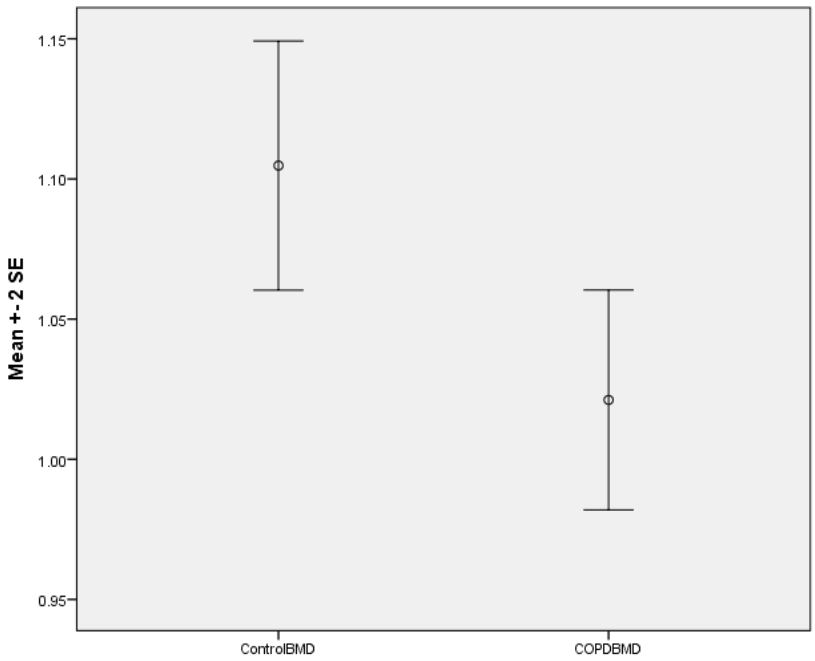


ControlPPT; Control group pressure pain threshold (n=53), COPDPPT; Control group pressure pain threshold (n=30)

Figure 18. Comparison of total PPT between COPD and control participants.

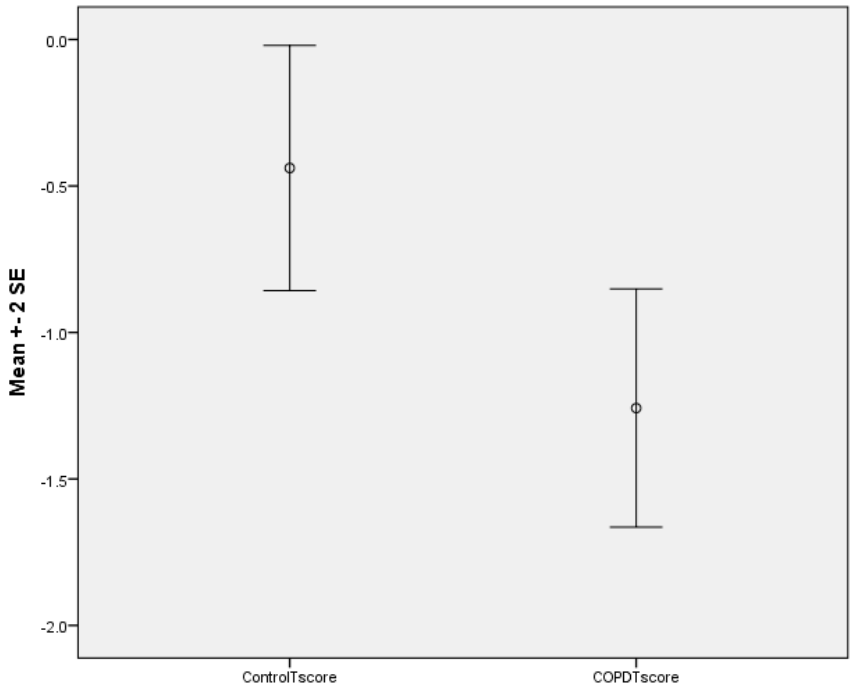
Bone Mineral Density

Bone mineral density was slightly higher in the control [1.07 gr/cm^2 (0.12)] compared to the COPD group [1.02 gr/cm^2 (0.11)], although the difference did not quite achieve statistical significance (p=0.09) (see Figure 19). Similar trends were seen for T-scores, with the mean T-score for those with COPD [-1.26 (1.13)] being within the published ranges for osteopenia (-1.00 to -2.5) and the mean control group results [-0.69 (1.19)] being within the range for normal, -1.00 or greater (WHO, 2003) (p=0.04). See Figure 20.



Control BMD; control group bone mineral density (n=53), COPDBMD; COPD group bone mineral density (n=31)

Figure 19. Comparison of bone mineral density between COPD and control participants.



TscoreControl; T-score control group (n=53), TscoreCOPD T-score COPD group (n=31)

Figure 20. Comparison of T-score between COPD and control participants

Other measures

Disability from spinal pain and pain bothersomeness measures using ODI, NDI and NRS scores did not differ statistically significantly between groups. The results from the COPD group did indicate mild disability in the cervical spine (NDI 12.12±15.24%) minimal disability with low back pain, (NDI 10.48±13.43%). In terms of bothersomeness of neck and back pain 70% and 64% of the COPD group reported bothersomeness of neck and back symptoms respectively, compared to 54% and 59% in the control group.

Finally, consistent with other literature in this field, scores for anxiety and depression (HADS) were significantly different ($p<0.001$) with scores of 7.71 (4.83) and 14.52 (6.82) in control and COPD groups respectively. These results indicate borderline 'abnormal' levels of anxiety and

depression in the control group and 'abnormal' levels in the COPD group (Zigmond & Snaith, 1983).

Correlations

A number of statistically significant bivariate associations between the two groups were found from correlation analysis of patient reported and performance-based measures of pulmonary function using Spearman's rho for non-normally distributed data (FEV_1/FVC, HAD, VAS scores) and Pearson's product moment correlation for normally distributed data of continuous variables (FEV_1 % predicted, FVC, all measures of spinal mobility, posture, bone mineral density and PPT). The main findings are summarised in text form below and supplementary results including analysis of sub groups based on disease severity as defined by GOLD are provided in appendix 16. Associations between FEV_1 % predicted (Table 16), MRC dyspnoea score (Table 17) and a range of other measures are provided.

Joint. No statistically significant associations were found for measures of pulmonary function and spinal mobility.

Posture. There was a weak negative correlation between C7-tragus posture and FEV_1% predicted (r=-0.38, p=0.04) in the COPD group compared to the control (r=0.09, p=0.53). A strong relationship between C7-tragus posture and lateral flexion was noted in the COPD group with most severe airflow obstruction, r=-0.9, p=0.04. It is however difficult to draw any firm conclusions with a sample size of 5 in this group.

Muscle pressure pain thresholds. Whilst a number of statistically significant associations were noted between measures of pulmonary function and PPT scores for the COPD group, these showed no consistent pattern across all muscles and low levels of association were observed for FEV_1% (left pectoralis minor; r=0.38, p=0.04, left scalene r=0.47, p=0.01). Across the control

group statistically significant, but weak negative correlations were noted for right trapezius; r=-0.27, p=0.05; right sternocleidomastoid; r=-0.31, p=0.03, left pectoralis minor; r=-0.31, p=0.03, and total score r=-0.28, p=0.04. For FVC only two statistically significant associations were found in the control group, left pectoralis minor; r=-0.29, p=0.04 and left trapezius; r=-0.28, p=0.04, again illustrating a low level of association.

A range of statistically significant negative associations between breathlessness, as measured using MRC dyspnoea scale and measures of PPT were observed in the COPD group, right and left pectoralis minor, r=-0.38 p=0.04 and r=-0.45 p=0.02 respectively, right and left trapezius, r=-0.48 p=0.01 and r=-0.47 p=0.01 respectively, right and left sternocleidomastoid, r=-0.50 p=0.01 and r=-0.51 p=0.004 respectively and right and left scalene, r=-0.44 p=0.02 and r=-0.45 p=0.01 respectively. The moderate to strong relationship seen between sternocleidomastoid and dyspnoea is unsurprising given our knowledge of its role as an accessory muscle of respiration.

Questionnaires. In the COPD group statistically significant yet low negative associations were found between T-score SGRQ activity score (r=-0.45, p= 0.01), SGRQ total score (r=-0.42, p= 0.02), indicating that bone mineral density is influenced by activity levels, with inactivity relating to reduced bone mineral density. Furthermore, a moderately strong positive correlation was observed for SGRQ activity score and HAD (r=0.60 p<0.001), which is interesting given the lack of published evidence linking depression and anxiety to physical activity levels in COPD. SGRQ total score was also positively and strongly associated with HAD (r=0.60 p <0.001), which is unsurprising given total score relates to overall status of respiratory health and includes elements of psychological status (Jones *et al.,* 1992). Further support for this is seen with FEV_1% predicted results showing a negative but low correlation with HAD (r=-0.36 p=0.04), and SGRQ total score r=-0.39 (p=0.03).

Table 13 provides an overview of bivariate correlations between FEV_1% predicted and a range of measures and presented based on GOLD sub groups. The only notable finding is the moderately strong negative association between FEV_1% predicted and SGRQ, ($r=-0.64$, $p<0.05$) for GOLD stage II, moderate disease severity.

With respect to associations between dyspnoea and measures taken, this provides some interesting findings, especially with respect to the moderate COPD group. Dyspnoea was positively strongly associated with SGRQ ($r=0.83$, $p<0.001$), HADS ($r=0.75$, $p<0.001$) and negatively associated with PPT ($r=-0.82$, $p<0.01$). To a lesser extent dyspnoea was associated with a forward head posture ($r=-66$, $p<0.05$) in GOLD stage II. See table 14 for association between breathlessness (MRC Dyspnoea Scale) and range of measures presented for sub groups based on GOLD criteria.

Table 13: Association between pulmonary function (FEV_1 % predicted) and range of measures for sub groups based on GOLD criteria

	GOLD 0 n=51	GOLD I n=17	GOLD II n=13	GOLD III n=6
Thoracic spine rotation	0.18	-0.09	-0.53	-0.35
Cervical spine rotation	-0.5	0.02	0.12	-0.64
Cervical spine lateral flexion	-0.08	-0.48	0.07	-0.67
T8-C7 to vertical (degrees)	-0.16	-0.10	-0.01	-0.15
C7-tragus to vertical (degrees)	0.09	-0.33	0.46	0.41
Tragus-eye to vertical (degrees)	-0.1	0.02	0.40	0.10
Total PPT	-0.09	0.22	-0.20	0.52
Bone mineral density	-0.11	0.01	0.18	-0.40
T score	-0.06	0.05	0.07	-0.40
Hospital Anxiety and Depression Scale	-0.35*	-0.42	-0.32	-0.64
SGRQ total	1.00**	-0.64*	0.12	-0.06
Steroids	-0.19	-0.74	0.44	-0.58
Smoking pack years	-0.27	-0.54	0.04	0.23
VASN	-0.26	-0.46	0.04	0.45
VASB	-0.07	-0.32	-0.32	-0.22

* significant at the level of 0.05 (2-tailed) ** significant at the level of 0.01 (2-tailed)

Table 14: Association between breathlessness (MRC Dyspnoea Scale) and range of measures sub groups based on GOLD criteria

	GOLD 0 n=51	GOLD I n=17	GOLD II n=13	GOLD III n=6
Thoracic spine rotation	-0.08	-0.19	-0.13	0.17
Cervical spine rotation	-0.38**	0.07	0.36	-0.17
Cervical spine lateral flexion	-0.25	0.66**	-0.04	-0.34
T8-C7 to vertical (degrees)	0.16	0.27	0.31	0.45
C7-tragus to vertical (degrees)	-0.08	0.21	**-0.66***	0.67
Tragus-eye to vertical (degrees)	-0.01	-0.01	0.26	-0.22
Total PPT	-0.09	-0.18	**-0.82****	-0.68
Bone mineral density	-0.04	-0.02	-0.24	0.26
T score	-0.13	-0.10	-0.54	0.26
Hospital Anxiety and Depression Scale	0.08	**0.49***	**0.75****	0.68
SGRQ total	-1.00**	0.48	**0.83****	0.34
Steroids	0.15	0.76**	0.51	0.51
Smoking pack years	0.39**	0.69	0.40	0.68
VASN	0.21	0.48	0.55	-0.50
VASB	0.17	0.12	0.31	0.00

- * significant at the level of 0.05 (2-tailed)
- ** significant at the level of 0.01 (2-tailed)

Having checked the data set for assumptions required to perform multiple regression analysis (multicollinearity, tolerance, normality, homoscedasticity, independence of residuals and presence of outliers), three outliers were identified and all other prerequisites met. Having evaluated the data with, and without, the outliers included, it was deemed appropriate to keep

outliers in for the remainder of the analysis given the limited influence on the preliminary results (including outliers the model R squared = 0.53; however, without outliers =0.53 where p=<0.001).

Relationship between lung function (FEV_1% predicted) and musculoskeletal parameters (Linear regression models)

The linear regression models showed that, whilst many of the predictor outcome measures, cervical motion, muscle sensitivity and some postural measures appear to have no statistically significant association with FEV_1% predicted values, thoracic spine rotation and C7-tragus posture were significantly associated with FEV_1% predicted across the whole sample.

Thoracic spine. 20% of the variance observed in FEV_1% predicted in our sample can be explained by the variables included in the model, which includes thoracic spine rotation, age, BMI, and sex. For each unit increase in FEV_1% predicted, there is 0.48 degree increase of thoracic rotation. When adjustments were made for additional covariates, HADS and smoking, this reduces to 0.31 degrees and 0.28 degrees respectively, with model remaining significant.

C7-tragus posture. In our minimally adjusted model it is seen that 5% of the variance in FEV_1% predicted can be explained by the model which includes C7-tragus posture, age, BMI, and sex. From model one, for each unit decrease in FEV_1% predicted, there is 0.23 degrees increase in C7-tragus posture (p=<0.05). Where adjustments were made for HADS and smoking, this increases to 0.27 degrees, with the model remaining significant (see Table 15).

Table 15. Linear regression model comparing FEV_1% predicted with musculoskeletal parameters.

	Model 1 (minimally adjusted BMI, age, sex)				Model 2 (adjusted HADS)				Model 3 (adjusted smoking)			
	β (95% CI)	P value	R^2	Adjust R^2	β (95% CI)	P value	R^2	Adjust R^2	β (95% CI)	P value	R^2	Adjust R^2
Thoracic spine rotation	0.48 (0.54, 1.31)	<0.001*	0.24	0.20	0.31 (0.23, 0.97)	0.005*	0.40	0.36	0.28 (0.18, 0.89)	0.008*	0.47	0.43
Cervical spine rotation	0.27 (0.06, 0.59)	0.018*	0.09	0.05	0.13 (-0.08, 0.39)	0.19	0.34	0.30	0.09 (-0.12, 0.33)	0.37	0.42	0.37
Cervical spine lateral flexion	0.14 (-0.13, 0.5)	0.25	0.05	0.002	0.03 (-0.23, 0.30)	0.78	0.37	0.33	0.03 (-0.21, 0.28)	0.79	0.46	0.42
Muscle sensitivity (PPT)	0.23 (0.00, 0.02)	0.04*	0.07	0.03	0.03 (-0.10, 0.01)	0.82	0.32	0.28	-0.03 (-0.01, 0.01)	0.75	0.41	0.37
Posture												
C7-tragus	-0.23 (-1.76, -0.02)	0.046*	0.09	0.05	-0.23 (-1.63, -0.13)	0.02*	0.34	0.29	-0.27 (-1.74, -0.35)	0.004*	0.45	0.40
Thoracic spine posture	-0.09 (-1.78, 0.81)	0.46	0.05	0.001	-0.01 (-1.2, 1.08)	0.92	0.29	0.24	-0.05 (-1.36, 0.80)	0.42	0.38	0.36
Tragus-eye	-0.06 (-1.11, 0.65)	0.61	0.05	-0.003	-0.04 (-0.90, 0.63)	0.73	0.29	0.24	-0.04 (-0.86, 0.58)	0.69	0.38	0.33

Musculoskeletal measures and their association with COPD (Logistic regression analysis)

In the multivariate analysis, there was a statistically significant association between having COPD and a reduction in thoracic spine rotation and increased angulation of C7-tragus posture. This was not the case, though, for cervical range of motion, muscle sensitivity and other postural measures.

Thoracic spine. In the minimally adjusted model (age, BMI and sex), there was a statistically significant association between thoracic spine rotation and having COPD (odds ratio 0.91; 95% CI 0.87-0.95). A similar size odds ratio was seen where adjustment was made for anxiety and depression and smoking respectively (odds ratio 0.90; 95% CI 0.84-0.97). (Table 16).

C7-tragus posture. C7-posture in the neck only appeared to be associated with having COPD once adjustment was made for age, BMI and sex, anxiety and depression and smoking. (OR 1.15; 95% CI 1.02-1.29).

Cox & Snell R squared and Nagelkerke pseudo R square values are reported to provide an indication of the variability of the dependant variable (COPD) explained by the factors in the model (Tabachnick & Fiddell, 2001). Therefore we can conclude that between 52% and 71% of the variability in model 3 is likely explained by the set of variables related to thoracic spine rotation. Likewise between 49% and 67% is likely explained by the variables for C7-tragus posture.

Sensitivity analysis

Using spirometry criteria, there were two patients with physician diagnosed COPD who had normal lung function, and 5 control participants who had airway obstruction consistent with COPD. The sensitivity analysis was undertaken for the logistic regression models where participants were reassigned to COPD or control based on the spirometry criteria. The

magnitude and direction of findings remained the same as the main analysis. The results are included in appendix 17.

Table 16. Association between COPD and musculoskeletal parameters based on logistic regression models.

	Model 1 (minimally adjusted sex, BMI, age)				Model 2 (adjusted HADS)				Model 3 (adjusted smoking)			
	OR (95% CI)	P value	C&S	Nagel.	OR (95% CI)	P value	C&S	Nagel.	OR (95% CI)	P value	C&S	Nagel
Thoracic spine rotation	0.91 (0.87,0.95)	<0.001*	0.26	0.35	0.92 (0.88,0.97)	0.002*	0.36	0.50	0.90 (0.84,0.97)	0.003*	0.52	0.71
Cervical spine rotation	0.98 (0.96,1.00)	0.01*	0.09	0.12	0.98 (0.96,1.00)	0.12	0.29	0.39	0.98 (0.96,1.01)	0.23	0.46	0.63
Cervical spine lateral flexion	0.99 (0.97,1.01)	0.31	0.04	0.05	1.00 (0.97,1.02)	0.69	0.28	0.38	0.99 (0.96,1.02)	0.55	0.48	0.65
Muscle sensitivity (PPT)	1.00 (1.00,1.00)	0.004*	0.13	0.17	1.00 (1.00,1.00)	0.06	0.30	0.41	1.00 (1.00,1.00)	0.27	0.46	0.63
Posture												
C7-tragus	1.05 (0.98,1.11)	0.15	0.06	0.08	1.05 (0.98,1.13)	0.16	0.26	0.36	1.15 (1.02,1.29)	0.02*	0.49	0.67
Thoracic spine posture	1.06 (0.96,1.15)	0.25	0.05	0.06	1.05 (0.94,1.17)	0.38	0.25	0.34	1.15 (0.98,1.35)	0.08	0.47	0.64
Tragus-eye	1.00 (0.95,1.07)	0.71	0.03	0.04	1.01 (0.94,1.08)	0.77	0.24	0.33	1.02 (0.93,1.11)	0.74	0.44	0.61

OR; odds ratio, C&S; Cox and Snell R square, Nagel.; Nagelkerke R square.

5.9. Discussion

Musculoskeletal changes are evident in patients with COPD. This study has described these differences in terms of static seated postural changes, reduced cervico-thoracic joint mobility, and increased accessory respiratory muscle sensitivity in patients with COPD compared to age- and gender-matched healthy participants. Moreover, thoracic axial rotation and cervical posture (C7-tragus) appeared to be associated with pulmonary function measure of FEV_1% predicted and having diagnosed COPD.

5.9.1. Spinal range of motion

Cervical ranges of motion (rotation and lateral flexion) were reduced in the COPD group compared to the control group although the difference failed to achieve statistical significance.

Thoracic axial rotation was significantly reduced in the COPD group by ~15-degrees and found to be associated with poorer pulmonary function across the whole sample from regression analysis. Furthermore, compared to those without a diagnosis of COPD, those with COPD had reduced thoracic mobility, and this association remained after adjustment for BMI, age, sex, HADS and smoking. Although reference is made to thoracic axial rotation, the derived measure of axial rotation was likely a product of rotation in the thoracic and lumbar spine based on the testing protocol used. Given the anatomical proximity of these spinal regions it was not possible to isolate thoracic spine motion from motion occurring in the five lumbar segments below. The relative contribution of each of these spinal regions to full axial rotation is unknown, although from Panjabi & White (1990) it appears the contribution from the lumbar spine is considerably less than that of the thoracic region. See figure 6, page 78.

Whilst there is little published evidence of a relationship between bony structure and thoracic mobility, it is reasonable to assert a link, given that biomechanically, structure and function are interdependent. In this study BMD was evaluated to enable comparison across groups.

Modelling to adjust for BMD was not performed due to the limited sample size and risk of over adjustment with the inclusion of BMI for modelling and a known relationship between weight and BMD (Zillikens *et al.,* 2010). During data collection it was noted that some of the COPD participants, but none of the controls, became breathless during thoracic motion testing, which may have contributed to the overall differences seen with structural compromise. Possible explanations for this include positional pulmonary compromise or fatigue, which is highly prevalent in COPD (Baltzan *et al.,* 2011). As a consequence, this may have resulted in an underestimation of the 'true' thoracic mobility for the COPD group, if limited by physiological compromise or psychological factors, rather than structural restriction. Lee *et al.,* (2010) suggest that axial rotation of the spine (and ribcage) may be limited to ensure ribcage compliance is not too severely compromised; where available joint is used to rotate, the remaining available range for respiration is reduced. Alternative structural explanations include loss of vertebral joint integrity secondary to undiagnosed vertebral compression fractures (Kjensli *et al*., 2009; Majumdar *et al.,* 2010) or postural differences not elicited from this research (Edmondston *et al.,* 2007).

5.9.2. Posture

Of the postural measures recorded, the only notable difference was an increased angle for C7-tragus in COPD participants compared to controls, consistent with a 'poking chin' posture. This lends some support to poorer pulmonary function being related to increased angulation at the C7-tragus level which is associated with a forward head posture. This finding is consistent with increased accessory respiratory muscle activity found in COPD airways (Gandevia *et al.,* 1996; de Andrade *et al.,* 2005) and postural adaptation to open the upper (Courtney, 2009).

Postural changes at C7-tragus were found to partly account for variance in pulmonary function observed across our sample, but was also found to be weakly associated with a diagnosis of COPD from logistic regression modelling. This is the first study to describe changes in sitting

posture in COPD, although comparison of sitting postures on pulmonary function and contributing factors to postural change, such as bony deformity, have previously been documented. Landers *et al.,* (2006) concluded that there was no difference in pulmonary function in different sitting postures in COPD. However, the use of a small sample and a crossover design in their study did not reflect habitual postures that may change over time and with disease progression. Standardisation of the overall sitting position was achieved across our sample; however spinal postures may only be partly correctable (towards the norm) given habitual changes over time. Kjensli *et al.,* (2009) reported significant structural differences in the vertebral bodies of COPD patients compared to controls. However, differences in thoracic posture were not seen in our study. This may be explained by our COPD sample being predominantly mild to moderate disease severity or the approach used to measure thoracic posture. Measurement of cervical posture is widely reported in the literature using digital images (Raine *et al.,* 1997; Silva *et al.,* 2010). However, this approach has not yet been validated for use in the thoracic spine. Increased accessory muscle activity, due to dyspnoea and hyperinflation (Peche *et al.,* 1996; de Andrade *et al.,* 2005; De Troyer *et al.,* 1994; Gandevia *et al.,* 1996) and postural adaption most likely accounts for increased C7-tragus angle or forward head posture seen in the COPD group. C7-tragus posture being associated with pulmonary function as seen with linear regression modelling and presence of COPD should not come as any surprise given the dyspnoea is associated with disease progression.

5.9.3. Muscle sensitivity

Pressure pain threshold testing showed an overall trend of lower thresholds indicative of heightened sensitivity in all muscles in the COPD group, with some muscles achieving statistically significant differences, but with no overall pattern evident. Total score for all measures did however show a statistically significant difference. We believe this is one of the first studies to have recorded PPT of accessory respiratory muscles in COPD, although research

exploring airway sensitivity in COPD and asthma patients reported similar trends with heightened levels of sensitivity and PPT of muscles in a mixed cohort of COPD and asthma patients (Johansson *et al.,* 2012). The inclusion of different muscles (supraspinatus, middle trapezius, thumb phalanx and gracilis muscle) and use of relatively younger participants (mean age ± standard deviation; COPD 63.9±5.8, controls 51.5±9.1) preclude direct comparison with the current study (Johansson *et al.,* 2012). Barbe & Barr (2002), in a review of work-related musculoskeletal dysfunction, concluded that raised levels of inflammation (local and possible systemic) are evident in participants performing repetitive and/or forceful tasks. Moreover, these inflammatory changes could account for the symptoms, including pain, observed in studies of work-related musculoskeletal dysfunction. It is therefore unsurprising to find changes in the sensitivity of these particular muscles, given the extent of accessory respiratory muscle use and systemic inflammation reported in COPD.

5.9.4. Bone mineral density

Bone mineral density scores were slightly but not statistically significantly lower for the COPD group compared to controls however the T-score was statistically different ($p=0.04$) with the COPD group having a score which is consistent with osteopoenia. These findings are consistent with other research despite having a population with lower disease severity (Jorgensen *et al.,* 2007; Kensli *et al.,* 2009) and reported prevalence rates of reduced bone mineral density estimated at 35.1% (range 9–69%) (Graat-Verboom *et al.,* 2009). Additionally the current study used a total body scan and a global score for BMD testing, where other studies have specifically used BMD results for localised regions, such as hip and lumbar spine (Silva *et al.,* 2011). In line with earlier reported results, no correlation was found between smoking-pack years and BMD for the COPD (Silva *et al.,* 2011).

5.9.5. Spinal disability

Measures of spinal disability (NDI and ODI) and NRS bothersomeness of neck and back complaints did not significantly differ between groups, nor did they show any relationship with pulmonary function. This, again, is unsurprising given that our sample was predominantly mild to moderate in severity. Nevertheless, the direction of effect again is suggestive of greater disability and bothersomeness of neck pain in the COPD group, with insufficient power to detect a statistically significant effect. This trend towards bothersomeness of neck pain in COPD group may be a consequence of accessory muscle recruitment and strain on musculoskeletal structures around the neck (Courtney, 2009).

With most research in COPD focused on symptomatic dyspnoea, research into pain is lacking. The prevalence of pain (predominantly in the neck, shoulders and chest) is, however, reported to be higher in COPD (45%) compared to the general population (34%) (Bentsen *et al.,* 2011). Pain is more likely associated with advanced disease progression, due to co-morbid musculoskeletal changes, although pain prevalence across disease severity and, in relation to known changes in the musculoskeletal system such as BMD, remains unknown.

Recent qualitative research suggests that pain of musculoskeletal origin, especially that originating in the neck, shoulders, and chest wall may be of significant clinical relevance for COPD management, although more likely associated with advanced disease progression (Lohne *et al.,* 2010). As our sample was predominantly in the mild to moderate stages, it was unlikely pain would be highly prevalent in our COPD sample, as was borne out with the results. With the additional work of breathing from accessory muscle recruitment in COPD and the resultant strain on structures around the neck, it is reasonable to assert that these participants may be at risk from developing neck pain. Future research using larger samples would be useful to explore the relationship between posture, pain and pulmonary function.

5.9.6. Additional observations

Depression and anxiety scores were significantly higher in the COPD group than the control group (p=<0.001). A negative correlation between anxiety and depression and FEV_1 % predicted as a measure of pulmonary function (r=-0.36, p=0.4) were noted for COPD group correlations.

5.9.7. Strengths and Limitations

Data collection was performed principally by the main researcher, an expert in musculoskeletal physiotherapy and trained in spirometry. Whilst the sample size was calculated *a priori*, it was based only on results from the reliability study (Heneghan *et al.,* 2009). In hindsight, it would have been useful to have considered calculating sample sizes for each of the predictor outcomes individually, and then using largest sample size calculated to ensure power was adequate for all outcomes and not just for the primary measure of thoracic mobility. Furthermore, whilst some sub-group analysis has been undertaken this was limited due to low numbers in each group when classified by disease severity.

Reliability data for the main outcome measure, thoracic motion was determined prior to the start of the study. This was done with a sample of young, healthy participants. Future research may usefully consider the stability of measures and reliability of the measurement approach in an older population, however the applicability of this approach as a measurement tool is questionable given the skills required for scanning, accessibility of equipment and practicalities of testing. It is however reasonable to suppose that reliability may be somewhat lower in older individuals, with likely degenerative changes in the spine that could compromise image acquisition of the laminae. Moreover, the previous repeatability study for thoracic motion analysis (Heneghan *et al.,* 2009) concluded that a mean measure of three provided the best outcome measure; this was in an asymptomatic population. Further research may usefully

consider whether a single measure may be sufficient given the observed breathlessness COPD participants experiences on repeated testing.

Participants were classified based on diagnosis at referral to the study, but not post-bronchodilator, which could result in some sample heterogeneity where asthma is not fully differentiated from COPD. However, the UK guidelines at the time of the study did not advocate post-bronchodilator spirometry for diagnosis of COPD (NICE, 2004). Participants in this study were recruited based on a medically supported diagnosis of COPD, however from spirometry testing it was evident that a number of participants who volunteered as COPD did not have spirometry results to support a diagnosis of COPD (n=2), and vice versa (n=5). This is unsurprising, given the high prevalence of under- and over diagnosed cases of COPD (Hill *et al.,* 2010).

Whilst a measure of depression and anxiety was included to enable comparison with other studies and allow statistical modelling, it may be useful to have included a measure of fatigue. The Multidimensional Fatigue Inventory (Lewko *et al.,* 2009) may have provided data to determine whether reduced motion was attributable to fatigue, which could occur in COPD group during physical activity. However, given a previous study has shown that anxiety relates closely to both fatigue and motivation (Wong *et al.,* 2010), one could assert that these two variables were partly accounted for with the inclusion of HADS, although in this study analysis for the anxiety subscale alone was not included.

Future research may usefully consider the use of an accelerometer to provide a performance-based measure of physical activity, rather than using a self-reported measure for just the COPD participants as was the case with this study, using the activity subscale of the SGRQ. Within the data analysis, we did not adjust for steroid use, as the data was inadequate being limited to 'courses per year' rather than a detailed knowledge of doses over a given period, which may

have been more precise and useful. However, guidance from existing research on how best to accurately calculate and adjust for steroid use was found to be lacking (Kjensli *et al.,* 2009).

Supplementary oxygen therapy during thoracic mobility testing may have been useful to minimise possible exercise-related anxiety and/or exercise-induced hypoxia. Such physiological (dyspnoea) or psychological factors (fear of dyspnoea) may have compromised COPD participants' motivation to push to end of available range of motion, resulting in an underestimation of actual available range of motion (Garrod *et al.,* 2000; Nonoyama *et al*., 2007).

Whilst the multivariate analyses examining the association between musculoskeletal changes and pulmonary function adjusted for a number of factors, including common known confounders, it must be acknowledged that there may be residual confounding with factors that have not yet been identified and have therefore not been controlled for in this analysis.

5.9.8. Implications

Current clinical practice of stable COPD is generally is focused on developing physiological capacity through physical exercise. This study provides evidence to support the inclusion of some flexibility or mobility exercises as an adjunctive intervention aimed at maintaining or increasing flexibility of the related regions. A well-designed, fully powered clinical trial is now required to systematically evaluate the effectiveness of a musculoskeletal flexibility programme in COPD, using validated patient-reported and performance-based outcome measures with short and long term follow up.

5.10. Conclusions

Whilst many of our musculoskeletal measures failed to demonstrate any statistically significant difference between controls and COPD participants, the overall trend was that participants with mild to moderately severe COPD had reduced spinal motion, postural changes and greater

accessory respiratory muscle sensitivity. Furthermore, a forward head posture and reduced thoracic joint mobility were found to be associated with reduced pulmonary function as measured using FEV_1% predicted, the most widely used outcome measure for clinical trials of COPD.

Chapter 6. DISCUSSION

The introduction of this thesis provided an overview of this debilitating disease, in terms of economics, clinical guidelines and evidence-based management options, ranging from pulmonary rehabilitation to manual therapy. A bias towards current management options focused on physiological principles was highlighted despite recognition of COPD as a complex multi-system disease with changes evident in the musculoskeletal system. Theoretically, changes to bone structure, joint mobility, and collagenous tissues of the thoracic cage may adversely affect respiratory biomechanics, as seen in restrictive pulmonary diseases, such as ankylosing spondylitis. With recent clinical guidelines (Bott *et al.,* 2009) highlighting the need to evaluate the effect of thoracic mobility exercises in COPD management, further research was clearly necessary. Planning this thesis required a review of the relevant musculoskeletal and respiratory literature to cover scope of available evidence to support the focus of this thesis which was included in Chapter 1.

Chapter 2 reported findings from a systematic review of passive intervention, manual therapy as a management approach for COPD (Heneghan *et al.,* 2012). The heterogeneity of interventions available and inconclusive findings highlighted a need to better understand the changes that occur in the musculoskeletal system in COPD, and how they may in themselves affect pulmonary function. Whilst the two intervention approaches reviewed, RMSG, an active intervention, and manual therapy, a passive intervention, included joint, muscle and soft tissue techniques, the underlying rationale for selection of techniques was universally underdeveloped. Furthermore evaluation of the effectiveness of any intervention aimed at increasing mobility is dependent on the availability of valid and reliable measurement tools. Measurement of flexibility in the thoracic region is technically challenging primarily due to the anatomical complexity of the many bones and joints which attach to form the rib cage. Cirtometry and motion analysis with skin sensors on the chest wall have been the main approaches used to examine chest wall

motion. However a synthesis of the evidence relating to the anatomy and coupled motion at the costovertebral and costotransverse joints during thoracic axial rotation offered an alternative approach to measurement of flexibility, drawing mainly on evidence from the musculoskeletal evidence base. With the majority of non-invasive approaches being used in the thoracic spine reliant on skin sensors doubt was raised as to the validity of such tools. Having reviewed the available range of thoracic motion analysis approaches in Chapter 3, it was evident that soft tissue artefact posed a significant threat to validity of current non-invasive techniques, which warranted further evaluation and quantification. Given significant soft tissue artefact during thoracic axial rotation was reported in Chapter 3 (Heneghan et al., 2010), a novel approach to motion analysis was developed using ultrasound imaging of the underlying bone, giving confidence that measurement was of the bone and not the skin. As with the development of any new tool this approach needed testing with respect to measurement properties. Although it was not possible to test validity against the accepted gold standard, use of imaging offered the prospect of improving on current approaches with visualisation of the bone being possible. For the purpose of this doctorate testing accuracy, stability of measures and reliability of a single tester was feasible. A sample of young adults was used to minimise potentially confounding influence of age, fatigue *etc.* This study was reported in Chapter 4.

Finally, in Chapter 5, a study is reported that set out to investigate the differences between participants with COPD and a control group using this new methodological approach. In addition to measuring thoracic mobility, other performance-based and patient-reported measurements of musculoskeletal and general function were made. Analysis included a description of the differences between the two samples and subsequent examination of any relationship between musculoskeletal measures, pulmonary function and a diagnosis of COPD. In summary, participants with COPD were found to have reduced spinal motion, altered posture and increased muscle sensitivity. Reduced active thoracic range of motion and an increased

angulation of neck posture were seen to be associated with both reduced pulmonary function and a diagnosis of COPD. The findings of this study provide some preliminary evidence that reduced pulmonary function in COPD is possibly restrictive as well as obstructive in nature. With current evidence-based management approaches focused on developing physiological capacity, these findings provide empirical evidence to support inception of a clinical trial of flexibility or mobility exercises in COPD.

With an ever growing COPD population and mounting medical and economic costs, the need to find alternative evidence-based management approaches is without question. Aside from smoking cessation, the main non-pharmacological evidence-based management of stable COPD is pulmonary rehabilitation, with physical exercise being considered the most beneficial element (ATS/ERS, 2006; GOLD, 2011). Although developing flexibility is not widely considered a key objective in pulmonary rehabilitation, a number of authors have proposed that interventions that enhance flexibility in the thoracic region in COPD may afford therapeutic benefit.

Until recently, little attention has been given to the extra pulmonary features of COPD, although this has changed with recognition that such co-morbidities, including those of the musculoskeletal system, may contribute significantly to the overall severity of the condition (GOLD, 2010). How exactly these relate to, and potentially influence pulmonary function in COPD has been a focus of this thesis, drawing on evidence from restrictive pulmonary diseases and evidence of musculoskeletal changes in COPD. The focus on flexibility as an adjunctive management approach is based on the premise that the chest wall, comprising a number of component parts, becomes stiff in COPD compared to healthy subjects, offering more resistance to muscles mobilising the thoracic cage associated with respiratory biomechanics (Estenne *et al.,* 1998). Whilst the underlying mechanisms are multifaceted, involving complex pathophysiological processes, the following section seeks to evaluate our findings in relation to existing evidence.

6.1. Joints

From our evaluation, cervical and thoracic spinal motion was seen to be reduced in subjects with COPD compared to control group, although only thoracic axial rotation demonstrated an association with pulmonary function and having COPD.

This is the first study to have evaluated thoracic axial rotation in COPD, although reduced axial rotation (at T8-9) has been reported to be significantly associated with reduced levels of vital capacity in a sample of adolescent, idiopathic thoracic scoliosis patients (n=109, mean age 14.2 years) (Takahashi *et al.,* 2007). Whilst idiopathic thoracic scoliosis does not constitute an obstructive pulmonary disorder, it does highlight a need to look beyond the lungs in COPD and consider whether a restrictive respiratory disorder may co-exist with the obstructive element of the disease, and partly account for compromised respiratory function in COPD. Whilst the focus for this thesis has been on musculoskeletal causes of restrictive pulmonary disorders there are an abundance of possible contributing factors that can lead to restrictive respiratory disorders in elderly subjects (Scarlata *et al.,* 2012). With COPD prevalence increasing with age, it is highly likely that subjects with COPD have some form of restrictive respiratory disorder as a result of aging alone, likely compounded further by the co-morbid extrapulmonary musculoskeletal features now widely recognised, such as osteoporosis, collagen degradation and vertebral bone deformities discussed earlier. Mannino *et al,* (2003), cited by Scarlata *et al.* (2012), reported prevalence of restrictive respiratory disorders being 6.6% in adults over 65 years, supporting further consideration of a co-existing restrictive respiratory disorders in COPD subjects. Their review identified an exhaustive list of causes of restrictive respiratory disorders, ranging from central nervous system multisystem atrophy to musculoskeletal disorders, such as ankylosing spondylitis and osteoporosis (Scarlata *et al.,* 2012). Whilst prevalence of restrictive respiratory disorders increases with advanced age, the authors of the review do suggest that targeted early management for vertebral osteoporosis may reduce the rate of decline, if not reverse deleterious

changes (Scarlata *et al.,* 2012). Whilst the authors did not elaborate on the nature of early management, drawing from the wider evidence base this could usefully include exercise. From a systematic review and meta-analysis of evidence (up to 2007) exercise was found to be beneficial with respect to improvements in physical function, pain, and vitality ($p<0.05$). Whilst only a small number of studies were included (n=4) and with just a total of 256 postmenopausal women with osteoporosis or osteopenia caution should be taken when drawing conclusions of the applicability to a wider population (Li *et al*., 2009).

Aside from any systemic inflammatory influence on individual joint, muscles, or supporting structures such as fascia, costal cartilages *etc.* (currently not known) greater involvement of the rib cage and accessory muscles for ventilation, as happens in COPD, may place strain on musculoskeletal structures contributing to tissue degeneration and in theory vice versa (Chaitow, 2002). Whilst breathing at rest relies predominantly on diaphragmatic excursion, it is reasonable to imagine that the abnormal repetitive strain on small joints of the rib cage secondary to increased activity of accessory muscles or strain may expedite the process of age-related joint degeneration and resultant joint stiffness (Barr & Barbe, 2002; Chaitow, 2002). As joint stiffness increases, resistance to movement also increases, which then requires greater muscle work to overcome the stiffness (Estenne *et al.,* 1998). In turn, this may then lead to deleterious changes to skeletal muscles acting on joints, with a vicious cycle of deteriorating respiratory biomechanics ensuing.

In terms of a comparison with other studies these results do illustrate a marked, but not unsurprising reduction in thoracic axial rotation with age with further notable attenuation in COPD. With many motion analysis studies measuring axial rotation in a young adult population, these results, notwithstanding different testing positions and measurement approaches, provide evidence of a marked reduction in thoracic mobility with age and respiratory disease, which as

discussed previously has the potential to affect respiratory function with altered biomechanics. Table 17 details a number of studies to enable comparison of results.

As discussed earlier the derived measure of axial rotation was likely a product of rotation occurring in the thoracic and lumbar spine regions. Although the testing protocol was developed following review of other measurement studies reporting thoracic motion (Willems *et al.,* 1996; Edmondston *et al,* 2007) it should be acknowledged that isolation of thoracic rotation from motion occurring in the lumbar region is debatable in the absence of additional imaging. Whilst the contribution from the lumbar spine is likely very small (Panjabi & White, 1990) this must be acknowledged and perhaps the term 'thoracolumbar' axial rotation would be a more appropriate term to use to describe spinal axial rotation.

Table 17: Comparison of motion analysis approaches and derived ranges of axial rotation

Author	Sample size and age	ROM: degrees mean (SD)	Measurement instrument	Testing position
Heneghan *et al,* 2010	24.96 (2.6) N=24	85.15 (14.8)	Ultrasound imaging & motion analysis	Arms overhead on bar
Heneghan *et al,* 2009	23.83 (3.1) N=30	74.62	Ultrasound imaging & motion analysis	Sitting Arms crossed
Willems *et al,* 1996	18-24 N=60 (30 males and 30 females)	Males 95.5 Females 88.2 Data based on sum of data for region motion (T1-4, T4-8, T8-12)	Fastrak and skin sensors	Sitting Arms crossed
Edmondston *et al,* 2007	18-43 years N=52	Estimated 81.8 40.0 (7.9) 95% CI 21.5 to 55.6) 41.8 (7.0) 95% CI 21.8 to 53.3)	Optical motion analysis system	Sitting arms held in 90-degrees horizontal abduction
Johnson *et al,* 2012	26.3 (4.3) N=46	Estimated total 81.6 40.8 (10.7) each way	Inclinometer	Lumbar locked position in prone kneeling
		Estimated total 121.2 60.6 (10.8) each way	Goniometer	Half kneeling -bar in front
		Estimated total 86.4 48.2 (10.7) each way	Goniometer	Half kneeling -bar behind
		Estimated total 82.2 41.6 (8.7) each way	Goniometer	Seated rotation-bar in back
		Estimated total 110.8 55.4 (9.2) each way	Goniometer	Seated rotation - bar in front
COPD **Chapter 5**	**67.22(8.52)** **N=33**	**38.77 (12.59)**	Ultrasound imaging & motion analysis	**Arms crossed**
Control **Chapter 5**	**66.58 (5.95)** **N=55**	**54.01 (15.67)**	Ultrasound imaging & motion analysis	**Arms crossed**

6.2. Posture

Whilst our study failed to detect a statistically significant difference between COPD and control subjects for two of our postural measures, a difference albeit not of statistical significance for C7-tragus posture was seen between the two groups. C7-tragus postural measure was also found to have a weak association with pulmonary function and a diagnosis of COPD. None of these findings should come as much of a surprise, given breathlessness is a hallmark of severe COPD. From sub group analysis of the current study (GOLD II group) breathlessness correlated moderately strongly to C7-tragus postural measure $r=-0.66$, $p=0.03$. Whilst this was not evident in the severe COPD it has to be remembered that this group had just 6 participants which was potentially insufficient to detect a meaningful difference. Changes in cervical posture may be a result of increased accessory respiratory muscle activity (de Andrade *et al.,* 2005), forward head posture to open the upper airways (Courtney, 2009), but also wider postural changes relating to bone and collagen degradation. Postural changes may be bony in origin, with reduced bone mineral density leading to anterior wedging of vertebral bodies, as observed in the osteoporotic spine (Widberg *et al.,* 2009). Bony changes and vertebral wedging in the thoracic spine can contribute to a forward head posture as a compensatory mechanism to facilitate forward vision, resulting in upper cervical extension and lower cervical flexion. Research of COPD subjects has shown evidence of vertebral body fractures (Majumbar *et al.,* 2010) and vertebral body deformities (Kjensli *et al*., 2009), both of which could influence static spinal posture. Flexed or kyphotic postures are widely reported in literature of ageing subjects, mainly women, and are a recognised risk factor for reduced pulmonary function (Scarlata *et al.,* 2012) although not supported with empirical evidence. Encouragingly though, results from a trial of exercise in healthy older women (mean age 72 years) found that a three-month multidimensional exercise programme, twice a week resulted in a reduction in kyphotic angle by 5-6 degrees ($p<0.001$). The programme incorporated strengthening, mobility and postural exercises focused on the trunk regions and upper limbs (Katzman *et al.,* 2007). The beneficial changes in thoracic

kyphosis were not seen in the cervical spine with neck posture not changing significantly, possibly a consequence of the bias in the exercise programme to mobility and strengthening exercises in the thoracic region. A useful addition would have been to include an evaluation of pulmonary function, as this would lend support for the development of a similar trial in COPD. Whilst subjects' age in the Katzman *et al.* (2007) study approximated our sample, measurement of spinal kyphosis differed with respect to approach and levels (T2-3 to T11-12) with our thoracic spinal postural measure being focused to the mid-upper thoracic region (T8-C7).

Research of musculoskeletal exercise interventions to improve pulmonary function in ankylosing spondylitis provides some support for the inception of a study to evaluate active exercise targeting this proposed co-existing restrictive element in COPD (Durmus *et al.,* 2009; Aytekin *et al.,* 2012). Two studies compared usual care with a 3-month home-based programme of spinal flexibility exercises (Durmus *et al.,* 2009; Aytekin *et al.,* 2012) and, in the case of Aytekin *et al.* (2012), they also had a third trial arm which comprised a Global Postural Re-education (GPR®) programme of equal duration. Both studies found significant improvements in pulmonary function, pain and flexibility in the interventions groups (Durmus *et al.,* 2009; Aytekin *et al.,* 2012). However, Aytekin *et al.* (2012) reported even more favourable results for the GPR® programme compared with the conventional spinal flexibility programme for improvements in pulmonary function. GPR® is a physical therapy method developed by Philippe-Emmanuel Souchard (France). The approach is founded on the basis that fascia exerts an influence on individual muscles that operate concurrently in body regions to facilitate functional movement, also known as 'kinetic chains'. These chains, by virtue of the fact that they comprise partly of non-contractile tissues are susceptible to adaptive shortening (Teodori *et al.,* 2011). The aim of GPR® programmes is to stretch the shortened kinetic chains using 15-20 minutes stretch holds in one of eight therapeutic postures; using the principles of creep, a property of viscoelastic tissue. This is in contrast to a more conventional stretching programme,

which targets muscles in isolation, using a timed period counted in seconds. Alongside stretching of shortened kinetic chains, GPR® aims to facilitate contraction of the antagonist muscles, aiming to minimise the development of postural asymmetry. Evaluation of the content of the GPR® programme would suggest the programme may be suitable for enhancing pulmonary function through the inclusion of specific strengthening and flexibility exercises of 'shortened' muscles, postural muscles, respiratory muscles and trunk muscles (GPR®, 2012). Aside from the extensive nature of the programme and significant differences in stretch duration, interestingly, GPR® does have some similarities to RMSG discussed in Chapter 1. Teodori *et al.* (2011) concluded from a systematic review of the available evidence that GPR® may enhance respiratory muscle strength and chest wall mobility, although detail for many included studies was lacking and the use of healthy subjects limits generalisability of findings to other groups. Furthermore, populations used in their review were heterogeneous ranging from chronic neck pain to women with urinary incontinence. No studies of GPR® in patients with respiratory disease or dysfunction have been identified.

6.3. Muscle

Despite considerable focus on skeletal muscle changes in COPD, little consideration has been given to describing changes that may influence muscle contraction beyond fibre type change (Orozco-Levi, 2003) such as muscle lengths, sensitivity *etc*. Given muscle sensitivity or pain can influence skeletal muscle contraction (Falla *et al.,* 2004; Dickx *et al.,* 2010) the reported exploratory observational study (chapter 5) sought to describe muscle sensitivity of accessory and associated respiratory muscles in COPD compared to healthy controls. The findings provide preliminary evidence that muscle sensitivity is heightened in COPD, which reflects other more recent research in COPD (Johansson *et al.,* 2012) and evidence from subjects performing repetitive and/or forceful tasks (Barbe & Barr, 2002). Whilst the reasons have not been elucidated from this study, it is reasonable to consider this multifaceted in nature, with postural changes, systematic inflammation, widely recognised in COPD, and a local inflammatory

response to repetitive activity contributing to the overall effect (Shah *et al.,* 2008). As our subjects were predominantly mild to moderate in disease severity and sample size was calculated based on thoracic spine data, it is therefore unsurprising these results did not achieve statistical significance.

Although not limited to pain of muscular origin, evaluation of musculoskeletal symptoms using numerical pain rating scale revealed slightly higher levels of reported bothersomeness of neck symptoms in the COPD group. The severity of the symptoms across the sample was generally low and reflected the low levels of neck-related functional disability seen as measured using NDI. To date, little research and clinical attention has been given to evaluating symptoms other than dyspnoea in COPD, although Bentsen *et al.* (2011) did report higher prevalence of pain, particular in the neck and shoulder regions in patients with COPD compared to a matched healthy group. Whilst we can't derive any firm conclusions from this, we could suggest that recruitment of, and increased workload of, accessory respiratory muscles in COPD may partly account for such symptoms, as proposed Barbe & Barr (2006). Additionally, levels of anxiety and depression may also affect accessory muscles with psychological status previously being shown to influence muscle sensitivity in women with chronic neck pain (Sjors *et al.,* 2011). One should be cautious, however, in generalising these findings to a COPD population. A useful addition to our work would have been to include pressure algometry measure of an unrelated respiratory muscle, such as a leg muscle (Sjors *et al.,* 2011). Measurement of tibialis anterior PPT in neck pain research has been done to assist differentiation of locally and centrally mediated pain mechanisms, with psychological factors contributing to centrally mediated pain mechanisms (Sjors *et al.,* 2011).

Grazzini *et al.* (2005) propose an overall shift in the relative contribution that respiratory muscles make to pulmonary function with advancing COPD. As disease severity increases, there is a relatively greater contribution to breathing from the accessory muscles of respiration, and a

greater involvement of the rib cage; a consequence of physiological and structural diaphragmatic insufficiency. Synthesising this with the evidence from this thesis, it would appear there is sufficient evidence to challenge the assertion of COPD as purely an obstructive pulmonary disease. This thesis has highlighted a need to continue to look beyond the lungs and consider a co-existent restrictive respiratory disorder in COPD. Asserting COPD as a mixed obstructive-restrictive lung disease has implications for both diagnosis and management. Whilst it goes beyond this thesis to discuss diagnosis in detail, evidence of a restrictive pulmonary disorder supports the recently revised guidelines for COPD diagnosis with the inclusion of assessment of co-morbidities such as osteoporosis and skeletal muscle dysfunction being indicated (GOLD, 2011). Diagnosis of COPD, based solely on spirometry measures of FEV_1, has the potential to overestimate the level of obstruction (and affect management decisions), in that FEV_1% predicted may be reduced as a result of both restrictive and obstruction elements (Gardner *et al.,* 2011).

In terms of management, it is interesting to note that there are several recent research reports evaluating the effectiveness of pulmonary rehabilitation in clinically diagnosed restrictive lung disease (Naji *et al.,* 2006; Kagaya *et al.,* 2009; Salhi *et al.,* 2010). Whilst results on the whole were favourable and comparable to results of pulmonary rehabilitation in COPD, recruitment was principally based on a restrictive pattern of ventilation from spirometry testing (Kagaya *et al.,* 2009; Salhi *et al.,* 2010). Consequently, there is considerable sample heterogeneity across studies of pulmonary rehabilitation in restrictive lung disease, ranging from interstitial lung disease (pulmonary fibrosis) to non-fibrotic restrictive lung diseases of musculoskeletal origin. Whilst this is justified on one hand to ensure a good sample size, it does then limit the strength of conclusions that can be made when discussing restrictive lung diseases of differing aetiology and mechanism. Common across all studies (Naji *et al.,* 2006; Kagaya *et al.,* 2009; Salhi *et al.,* 2010) and, in line with other studies of pulmonary rehabilitation, the exercise component of

pulmonary rehabilitation was focused on developing physiological capacity (Naji *et al.,* 2006; Kagaya *et al.,* 2009; Salhi *et al.,* 2010). Justification for rehabilitation being 'solely' focused on developing physiological capacity is questionable where the majority of the sample in one study had restriction of musculoskeletal origin; n=20 from a total sample n=31 had chest wall disease, such as kyphoscoliosis (Salhi *et al.,* 2010). Naji *et al.,* (2006) did, however, differentiate between subjects with interstitial lung disease and skeletal abnormalities, although, with small numbers in each group (n=11, n=4 respectively) and high attrition, they concluded there was much still to be learned, including a question linked to appropriateness of one programme for both groups. Perhaps this, along with findings from this thesis, provides evidence to further consider the scope and nature of the exercise component of pulmonary rehabilitation in clinical practice. It is however debateable what tools would be used to evaluate an effect given the age of the population, likely prevalence of a significant number of musculoskeletal co-morbidities and lack of published data on minimal clinical important differences for measures in that age group. From what was learnt from the evidence syntheses of manual therapy interventions (Heneghan *et al.,* 2012) perhaps evaluation of any trial should focus on patient reported measures of well-being such as quality of life, breathlessness *etc.* measures that have also been associated with disease progression and mortality.

6.4. Summary

There is a small body of evidence which has sought to evaluate the adjunctive use of a flexibility exercise programme in promoting respiratory biomechanics in the form of RMSG in COPD and GPR® in healthy subjects. Whilst COPD is primarily an obstructive lung disease, this thesis has provided preliminary evidence to suggest a co-existing restrictive element, resulting from changes in the musculoskeletal system. In synthesising the results from chapter 5 with evidence from management of ankylosing spondylitis, an extreme example of restrictive respiratory disorder, there appears sufficient evidence to support the inception of a clinical trial of flexibility

exercises in COPD. Whilst current clinical guidelines advocate research of thoracic mobility exercises, this appears too narrow given the evidence this thesis presents in terms of wider cervico-thoracic musculoskeletal changes and their association with pulmonary function and COPD. A clinical trial of pulmonary rehabilitation with adjunctive flexibility exercises, akin to those included in the GPR®, compared to standard pulmonary rehabilitation is now required to evaluate this idea. Should the adjunctive use of flexibility exercises afford greater therapeutic effect than pulmonary rehabilitation alone, then this would only serve to provide further evidence of COPD having both obstructive and restrictive elements.

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Appendix 1. Joints of the thorax

Joint (and joint type)	Articulation	Ligaments	Comments
Intervertebral	Adjacent vertebral bodies bound together by IV disc	Anterior & posterior longitudinal	
Joints of head of rib ***Synovial plane joint***	Head of each rib with superior demifacet or costal facet of corresponding vertebral body & inferior demifacet or costal facet of vertebral body superior to it	Radiate & intra-articular ligaments of head of rib. See	Heads of 1st, 11th, & 12th ribs (sometimes 10th) articulate only with corresponding vertebral body
Costotransverse ***Synovial plane joint***	Articulation of tubercle of rib with transverse process of corresponding vertebra	Lateral & superior costotransverse	11th & 12th ribs do not articulate with transverse process of corresponding vertebrae
Costochondral ***Primary cartilaginous joint***	Articulation of lateral end of costal cartilage with sternal end of rib	Cartilage & bone bound together by periosteum	No movement normally occurs at this joint
Interchondral ***Synovial plane joint***	Articulation between costal cartilages of 6th & 7th, 7th & 8th, & 8th & 9th ribs	Interchondral ligaments	Articulation between costal cartilages of 9th & 10th ribs is fibrous
Sternocostal ***1st: primary cartilaginous joint (synchondrosis)***	Articulation of 1st costal cartilages with manubrium of sternum		
2nd to 7th: synovial plane joint	Articulation of the 2nd to 7th pairs of costal cartilages with sternum	Anterior & posterior radiate sternocostal	
Sternoclavicular ***Saddle type of synovial joint***	Sternal end of clavicle with manubrium of sternum & 1st costal cartilage	Anterior & posterior sternoclavicular ligaments; costoclavicular ligament	
Manubriosternal ***Secondary cartilaginous joint (symphysis)***	Articulation between manubrium & body of sternum		Often fuses in older individuals
Xiphisternal ***Primary cartilaginous joint (synchondrosis)***	Articulation between xiphoid process & body of sternum		

Appendix 2. Muscle attachment to thoracic cage and respiratory muscles

Muscle name	Location	Action
Sternocleidomastoid	Neck	Lifts thorax during forced inspiration *if* head is fixed
Scaleni		Elevate first and second ribs when they take fixed point from above during forced inspiration
Trapezius	Upper and back part of neck & shoulders	Forced Inspiration
Rhomboideus Major	Between spine & shoulder blades	
Rhomboideus Minor		
Ilio-Costalis	Parallel to the spine; outermost on the back	Aids forced inspiration by fixing last rib
Latissimus Dorsi	Lower Back	Raises lower ribs to assist forced inspiration *if* the arms are fixed
Serratus Posticus Supior		Elevates ribs in forced inspiration
Serratus Posticus Inferior		Draws lower ribs downward and backward, and thus elongates the thorax (chest)
Pectoralis Major	Upper & Fore part of Chest	*When arms are fixed*, draws ribs upward during forced inspiration.
Pectoralis Minor	Upper & Fore part of Chest Beneath Pectoralis Major	Aids Pectoralis Major
Subclavis	Between clavicle and first rib	Works in conjunction with Pectoralis Major & Minor
Levatores Costarum	Sides of Chest to front of ribs	Assist in raising the ribs during forced inspiration
Triangularis Sterni	Inner wall of front of chest	Draws down ribs during forced expiration
External Intercostals	**Outside layer of Intercostals between the ribs**	**Raise the ribs during forced inspiration**
Internal Intercostals	**Inside Layer of intercostals between the ribs**	**Depress and invert lower borders of ribs during forced expiration. At fore part of chest they assist external intercostals during forced inspiration.**
Diaphragm	**Separates chest cavity from abdominal cavity**	**Increases vertical dimensions of the chest cavity during inspiration by flattening when it contracts. *It is relaxed during expiration.***
Quadratus Lumborum	Abdomen between pelvis & last rib	Aids forced inspiration by fixing last rib
Obliquus Externus	abdomen	They compress the lower part of the chest during forced expiration *if* the pelvis and spine are fixed.
Obliquus Internus		
Transversalis		
Pyramidalis		
Rectus Abdominus		
Levator Ani	Forms floor of pelvis	A muscle of forced expiration

Appendix 3. Musculoskeletal changes in COPD

Title	Author and date	Design	Sample	Outcome measures	Results	Comments
Structural changes of the thorax in COPD	Walsh J. *et al.* 1992	Case control	**COPD:** n=22 FEV_1 34±12 Hyperinflated 64±5 years **Normal**: n=10 62±6 years FEV_1 105±10	**X-Ray** performed at TLC, FRV & RV -Rib cage dimension (lateral diameter, rib angle, AP diameter) -Diaphragm position (AP & lateral x-ray)	No difference in rib cage dimension at all volumes Diaphragm significantly lower COPD **Overall conclusion**: changes confined to diaphragm	Small sample and no details on recruitment Supine lying No *a prior* power calculation
Relationship between thoracic cross-sectional area measured on CT and pulmonary function or dyspnea in patients with COPD	Kasai T *et al.* 2003	Descri ptive	**COPD:** n=24 FEV_1 34±12	**CT** performed at TLC, FRV & RV	Good correlation between TCSA and -total lung capacity ($r = 0.65$, $p < 0.001$) - functional residual capacity ($r = 0.67$, $p < 0.001$) -residual volume ($r = 0.62$, $p < 0.005$) **Overall conclusion**: Hyperinflation data (Pulmonary function data and TCSA) increased in patients with severe dyspnoea.	Small sample and no details on recruitment No *a prior* power calculation

Abdominal muscle use during breathing in patients with chronic airflow	Ninane V. *et al.* 1992	Case control	**COPD:** n=40 FEV_1 17-82% **Control:** n=12	EMG (US guided needle) Rectus abdominis External abdominal oblique Transversus abdominus During rest breathing supine and seating	COPD Rectus abdominis & External abdominal oblique silent Transversus abdominus: variable phasic activity during expiration n=17. Related to degree of obstruction ($p<0.005$). Sup and Seated In n=4 subjects diaphragm activity at same time as scalene activity during inspiration, but never with Transversus abdominus **Overall conclusion**: Stable patients with airflow obstruction contract abdominal muscles, usually Transversus abdominus.	Validity of measures given cross talk Potential for discomfort which could affect muscle fibre recruitment No *a prior* power calculation Wide range of severity
Neck muscle activity in patients with severe COPD	De Troyer A. *et al* 1994	Descri ptive	**COPD:** stable n=40 FEV1 0.69±0.18 (n=17 hypercapnic at rest)	EMG – needle • Scalene • SCM • Trapezius Seated and supine breathing at rest	Seated position: all patients use scalene for inspiration, none for trapezius, n=4 for SCM Supine: Trapezius and SCM silent despite dyspnea **Overall conclusion**: Most stable patients with COPD do not use SCM or trapezius when breathing at rest.	Small sample and no details on recruitment Discomfort with needle insertion reported No *a prior* power calculation

Discharge frequencies of parasternal intercostal and scalene motor units during breathing in normal and COPD subjects	Gandevia SC. et *al* 1996	Case control	**COPD:** n= 7 FEV_1 33±13% **Control**: n=7	EMG – needle Discharge frequency of single motor units of **scalene and 2nd parasternal intercostal** muscle US guided EMG needles during quiet breathing.	SCM silent in both groups during quiet breathing in COPD. Mean discharge frequency higher in COPD than normal for scalene ($p<0.02$) and second parasternal muscle ($p<0.05$) **Overall conclusion:** SCM is silent at rest, and there is greater activity in scalene and second parasternal intercostal muscle in COPD.	Small sample and no details on recruitment Discomfort with needle insertion reported No *a prior* power calculation
Sternomastoid muscle size and strength in patients with severe COPD	Peche R. *et al.* 1996	Case control	**COPD**: n=10 FEV_1 0.76±0.12 hyperinflation (FRC 210± 29%) **Normal:** n=10 Matched for age, sex and height	CT to measure CSA **SCM** SCM - Length Torque – Cybex dynamometer	**CSA** COPD 4.29±1.48 cm^2 Normal 3.96 cm^2 ($p>0.05$) **Torque:** similar once length accounted for (not reported in abstract) **Length:** SCM **shorter** in COPD patients compared to controls 127 and 140mms respectively $p<0.05$ **Overall conclusion**: In patients with severe COPD SCM muscles are much the same.	Small sample and no details on recruitment No *a prior* power calculation

Inspiratory muscular activation during threshold therapy in elderly healthy and patients with COPD	de Andrade A. *et al.* 2005	Case control	**COPD** n=7 66±8 years, FEV_1 45±17%, MIP 75.3 **Normal**: n=7 68±4 years	Surface EMG: **diaphragm, SCM** During 30% threshold load training	COPD: SCM ↑ activation (28%) to overcome Threshold load (diaphragm constant) Normal: diaphragm (11%) & SCM (7%) ↑ SCM – correlation (r=-0.537) with obstruction level **Overall conclusion**: COPD patients increase accessory muscle activity to overcome load; which also seems to be proportional to degree of obstruction	Small sample Potential for crosstalk with EMG EMG affected by multiple variables such as subcutaneous fat No *a prior* power calculation
An anatomic investigation of the serratus posterior superior and serratus posterior inferior muscles	Loukas M. *et al.* 2008	Case control	**COPD**: n=18 (6 male) Cadavers **Control**: n=32 Cadavers (58-82 years)	**Serratus Posterior Inferior & Superior** Muscle length, thickness, width	No morphometric differences (>0.05 students t-tests) **Overall conclusion:** no respiratory function be attributed to either these muscles	Small sample In vitro Not a widely considered respiratory muscle No *a prior* power calculation
Respiratory muscle activity and dyspnea during exercise in chronic obstructive pulmonary disease	Duiverman ML. *et al.* 2009	Case control	**COPD**: n=17 (9 male) 60 (54-64) years FEV_1% 32 (22-39) **Control**: n=10 (6 male) 55 (53-59) years FEV_1% 107 (93-117)	Surface EMG: **Scalene and intercostal muscles**	Scalene and intercostal activity increased immediately after onset exercise, where controls it increased > half way through exercise. **Overall conclusion:** Scalene and intercostal activity increased at a greater rate early in exercise compared with control	Small sample Potential for crosstalk with EMG EMG affected by multiple variables such as subcutaneous fat No *a prior* power calculation

The prevalence of osteoporosis in patients with COPD: a cross sectional study	Jorgensen N. *et al.* 2008	Cross sectional study	**COPD** n=62 FEV_1 % 32.6±14.1 Age 63.2±5.4 Male n=16	X-ray and DEXA scan lumbar spine and hip	68% osteoporotic, but not attributable to oral corticosteroid use Previously undetected fractures: n=15 Osteoporosis n=22 Osteopenia n=16 **Overall conclusion**: There is a need to screen COPD patients and to initiate management based on these findings	No *a prior* power calculation No gender and age match controls
High prevalence of vertebral deformities in COPD patients: relationship to disease	Kjensli A. *et al.* 2009	Cross sectional	**COPD**: n=88 recruited from sample 363 age 62.9±9.3 **Study group:** age 63.9±10.2 Male n=57	**Dimension of vertebral segments** using radiographic images	**COPD** 31% vertebral deformities **Controls** 18% (p<0.0001) **COPD GOLDII to III** – 2-fold increase in vertebral deformities **Overall conclusion**: Prevalence of vertebral deformities is higher in COPD after adjustment for risk factors & related to disease severity.	Unable to be confident about precision of data on use of corticosteroid Higher proportion of men in study group

AP; anterior-posterior, COPD; chronic obstructive pulmonary disease, CSA; cross sectional area, CT; computerized tomography, EMG; electromyography, FRV; functional residual volume, RV; residual volume, SCM; sternocleidomastoid, TLC; total lung capacity, US; ultrasound,

Appendix 4. Heneghan *et al.,* 2012

Appendix 9 Research protocol

Study Protocol

Purpose

The overall purpose of the research is to advance our understanding of how and to what extent the musculoskeletal system adapts/changes in the presence of chronic pulmonary disease, a progressive and debilitating lung disease. A secondary purpose is to understand whether or not such changes may be related to in the severity of lung function abnormality.

Much of the research in this field to date has focused on intrinsic changes to skeletal muscle due to the systemic inflammation that occurs as part of the disease process. There is evidence that posture and the associated chest wall muscles change in COPD and this is progressive with the disease process. However to date there has been little consideration of how other structures of the musculoskeletal system, such as joints may also change. Furthermore it is unclear whether such changes may also impact on the overall function of patients with COPD. This study will enable us to have a clearer understanding of how the musculoskeletal system changes in COPD compared to the normal aging process, and whether there is an association between structural change and lung function. With a better understanding of the nature and extent of such changes in the musculoskeletal system further research could then evaluate interventions aimed at treating or managing such biomechanical changes in breathing on function (respiratory and or lifestyle).

Primary aim

To identify the range and extent of differences in the musculoskeletal system, including spine movement and muscle length, in the presence of chronic obstructive pulmonary disease compared to a matched group of healthy subjects

Secondary aim

To evaluate possible relationships between the extent of any such musculoskeletal differences and the level of severity of lung function abnormality.

Method

Design

This is a case control study to determine the scope and nature of musculoskeletal changes that may occur in patients with chronic obstructive lung disease.

Sample

Purposive sample of subjects with stable COPD – mild-moderate airflow obstruction (30-80% predicted FEV_1) (NICE Classification, 2004) and a matched control group of healthy subjects will be used to compare musculoskeletal changes

Inclusion criteria; Cases: Moderate and stable COPD as per NICE Classification, Controls: Matched by age (+/- 5 years) and sex to each case. Both cases and controls: can speak English

Exclusion criteria; subjects with previous neuromusculoskeletal spine trauma or other relevant pathology, systemic rheumatological condition, who have undergone abdominal, lung or spinal surgery, have had a recent infection (last 6 weeks) or pregnancy.

Ethics

Ethical approval will be sought through the National Research Ethics Service. Risk assessment has been performed with appropriate use of participant information sheets, consent forms and subject information sheets. Subjects' anonymity will be maintained throughout using a coding system which will be maintained by the lead researcher ion a password protected file. Subjects will be assured that at no point would findings from the study be identifiable to themselves throughout the process of analysis and dissemination.

Recruitment

Local healthcare providers (GP, Respiratory Physicians, Physiotherapy Units) have been involved in the developing of this project through consultation and invited to support this study and letters of support are available.

British Lung Foundation has also offered local support through provision of local group details and introduction to organisers.

- Methods
    - Posters in clinics, health centres
    - Via GPs in South Birmingham from letter to GP
    - Invitation via BLF Newsletter

Subjects will be invited to participate and then will be followed up by the lead researcher. Subjects will then have the information regarding the study fully explained and given the opportunity to ask any questions. Subjects will be free to withdraw from the study at any point without having to provide any reason or affecting any ongoing management they may require.

The findings from the study will be made available to the GPs and subjects who participate in the study.

Procedure

Participants will be invited to complete the questionnaires prior to attendance for testing.

Questionnaires

- Medical Research Council dyspnea scale
- Hospital Anxiety and Depression Score (HADS)
- Neck Disability Index (NDI)

- Oswestry back disability index (ODI)

- St Georges Respiratory Questionnaire SGRQ (For COPD group only)
- COPD self efficacy (For COPD group only)

Then during a single visit assessment subjects will have a brief health questionnaire to complete and testing performed. It is estimated that the examination will take no more than 90 minutes. The choice of outcomes has been informed by a review of the current literature and in view of the potential limitations in exercise tolerance for the COPD group. Testing will for the most part take place in a supported seated position.

Measures of lung function

- **FEV_1 -** the forced expired volume from a full lung over the first one second of exhalation
- **FVC -** the forced vital capacity or maximum volume of air that a full lung can exhale.
- **Resting arterial saturation using pulse oximetry**

Primary outcome measures

- **Range of motion of neck and back** using motion analysis equipment
- **Shoulder and neck posture** using photographic images

Secondary outcome measures

- **Muscle length** using manual testing

- **Muscle sensitivity** using pressure algometer

- **Muscle Strength** using hand grip

Covariates

1. **Bone mineral density –DEXA scan**

2. **BMI**

Appendix 10. Hospital Anxiety and Disability Scale

Chart 1 – Hospital Anxiety and Depression Scale

This questionnaire will help your physician to know how you are feeling. Read every sentence. Place an "X" on the answer that best describes how you have been feeling during the LAST WEEK. You do not have to think too much to answer. In this questionnaire, spontaneous answers are more important.

A 1) I feel tense or wound up:
- 3 ( ) Most of the time
- 2 ( ) A lot of the time
- 1 ( ) From time to time
- 0 ( ) Not at all

D 2) I still enjoy the things I used to enjoy
- 0 ( ) Definitely as much
- 1 ( ) Not quite so much
- 2 ( ) Only a little
- 3 ( ) Hardly at all

A 3) I get a sort of frightened feeling as if something awful is about to happen
- 3 ( ) Very definitely and quite badly
- 2 ( ) Yes, but not too badly
- 1 ( ) A little, but it doesn't worry me
- 0 ( ) Not at all

D 4) I can laugh and see the funny side of things
- 0 ( ) As much as I always could
- 1 ( ) Not quite as much now
- 2 ( ) Definitely not so much now
- 3 ( ) Not at all

A 5) Worrying thought goes through my mind
- 3 ( ) A great deal of the time
- 2 ( ) A lot of the time
- 1 ( ) From time to time but not too often
- 0 ( ) Only occasionally

D 6) I feel cheerful
- 3 ( ) Not at all
- 2 ( ) Not often
- 1 ( ) Sometimes
- 0 ( ) Most of the time

A 7) I can seat at ease and feel relaxed
- 0 ( ) Definitely
- 1 ( ) Usually
- 2 ( ) Not often
- 3 ( ) Not at all

D 8) I feel as I am slowed down
- 3 ( ) Nearly all the time
- 2 ( ) Very often
- 1 ( ) Sometimes
- 0 ( ) Not at all

A 9) I get a sort of frightened feeling like butterflies in the stomach
- 0 ( ) Not at all
- 1 ( ) Occasionally
- 2 ( ) Quite often
- 3 ( ) Very often

D 10) I have lost interest in my appearance
- 3 ( ) Definitely
- 2 ( ) I don't take so much care as I should
- 1 ( ) I may not take quite as much care
- 0 ( ) I take just as much care as ever

A 11) I feel restless, as if I had to be on the move
- 3 ( ) Very much indeed
- 2 ( ) Quite a lot
- 1 ( ) Not very much
- 0 ( ) Not at all

D 12) I look forward with enjoyment to things
- 0 ( ) As much as I ever did
- 1 ( ) Rather less than I used to
- 2 ( ) Definitely less than I used to
- 3 ( ) Hardly at all

A 13) I get sudden feeling of panic
- 3 ( ) Very often indeed
- 2 ( ) Quite often
- 1 ( ) Not very often
- 0 ( ) Not at all

D 14) I can enjoy a good TV or radio program or book
- 0 ( ) Often
- 1 ( ) Sometimes
- 2 ( ) Not often
- 3 ( ) Very seldom

Appendix 11. Medical Research Council dyspnoea scale

Grade	Degree of breathlessness related to activities
1	Not troubled by breathlessness except on strenuous exercise
2	Short of breath when hurrying or walking up a slight hill
3	Walks slower than contemporaries on level ground because of breathlessness, or has to stop for breath when walking at own pace
4	Stops for breath after walking about 100m or after a few minutes on level ground
5	Too breathless to leave the house, or breathless when dressing or undressing

Adapted from Fletcher CM, Elmes PC, Fairbairn MB et al. (1959) The significance of respiratory symptoms and the diagnosis of chronic bronchitis in a working population. British Medical Journal 2:257-66.

Appendix 12.Neck Disability Index

Please Read: This questionnaire is designed to enable us to understand how much your neck pain has affected your ability to manage everyday activities. Please answer each Section by circling the **ONE CHOICE** that most applies to you. We realize that you may feel that more than one statement may relate to you, but Please **just circle the one choice which closely describes your problem *right now*.**

SECTION 1--Pain Intensity

I have no pain at the moment

The pain is mild at the moment.

The pain comes and goes and is moderate.

The pain is moderate and does not vary much.

The pain is severe but comes and goes.

The pain is severe and does not vary much.

SECTION 2--Personal Care (Washing, Dressing etc.)

I can look after myself without causing extra pain.

I can look after myself normally but it causes extra pain.

It is painful to look after myself and I am slow and careful.

I need some help, but manage most of my personal care.

I need help every day in most aspects of self-care.

I do not get dressed, I wash with difficulty and stay in bed.

SECTION 3--Lifting

I can lift heavy weights without extra pain.

I can lift heavy weights, but it causes extra pain.

Pain prevents me from lifting heavy weights off the floor but I can if they are conveniently positioned, for example on a table.

Pain prevents me from lifting heavy weights, but I can manage light to medium weights if they are conveniently positioned.

I can lift very light weights.

I cannot lift or carry anything at all.

SECTION 4 --Reading

I can read as much as I want to with no pain in my neck.

I can read as much as I want with slight pain in my neck.

I can read as much as I want with moderate pain in my neck.

I cannot read as much as I want because of moderate pain in my neck.

I cannot read as much as I want because of severe pain in my neck.

I cannot read at all.

SECTION 5--Headache

I have no headaches at all.

I have slight headaches which come infrequently.

I have moderate headaches which come in-frequently.

I have moderate headaches which come frequently.

I have severe headaches which come frequently.

I have headaches almost all the time.

SECTION 6 -- Concentration

I can concentrate fully when I want to with no difficulty.

I can concentrate fully when I want to with slight difficulty.

I have a fair degree of difficulty in concentrating when I want to.

I have a lot of difficulty in concentrating when I want to.

I have a great deal of difficulty in concentrating when I want to.

I cannot concentrate at all.

SECTION 7--Work

I can do as much work as I want to.

I can only do my usual work, but no more.

I can do most of my usual work, but no more.

I cannot do my usual work.

I can hardly do any work at all.

I cannot do any work at all.

SECTION 8--Driving

I can drive my car without neck pain.

I can drive my car as long as I want with slight pain in my neck.

I can drive my car as long as I want with moderate pain in my neck.

I cannot drive my car as long as I want because of moderate pain in my neck.

I can hardly drive my car at all because of severe pain in my neck.

I cannot drive my car at all.

SECTION 9--Sleeping

I have no trouble sleeping

My sleep is slightly disturbed (less than 1 hour sleepless).

My sleep is mildly disturbed (1-2 hours sleepless).

My sleep is moderately disturbed (2-3 hours sleepless).

My sleep is greatly disturbed (3-5 hours sleepless).

My sleep is completely disturbed (5-7 hours sleepless).

SECTION 10--Recreation

I am able engage in all recreational activities with no pain in my neck at all.

I am able engage in all recreational activities with some pain in my neck.

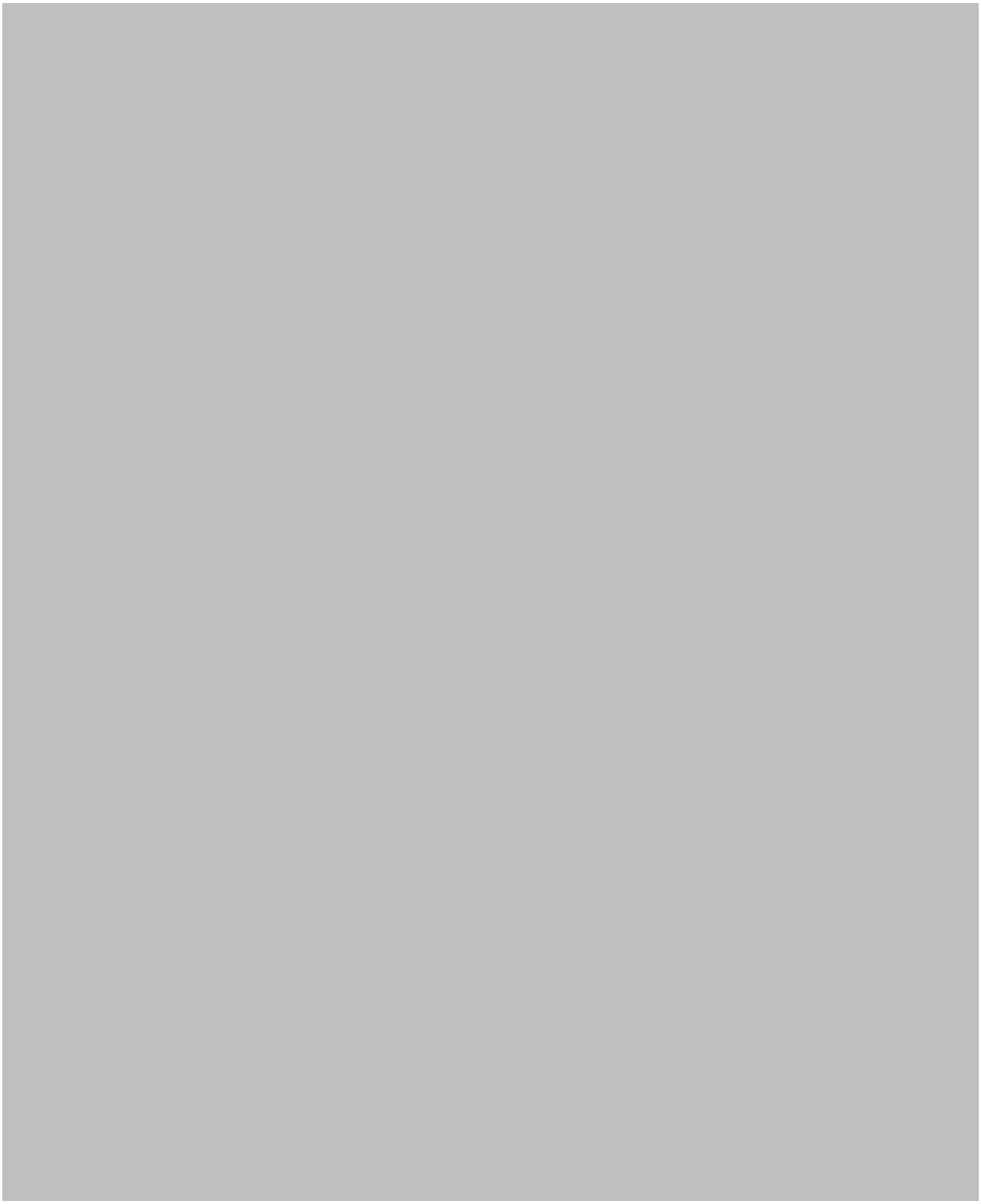
I am able engage in most, but not all recreational activities because of pain in my neck.

I am able engage in a few of my usual recreational activities because of pain in my neck.

I can hardly do any recreational activities because of pain in my neck.

I cannot do any recreational activities all.

Appendix 13 .Oswestry Disability Index



Appendix 14. General Health Questionnaire

Descriptive study of the skin movement occurring (relative to bone) during thoracic spine axial motion

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Name: .....

Address: .....

.....

Name of the responsible investigator for the study:

Nicola Heneghan

Please answer the following questions. If you have any doubts or difficulty with the questions, please ask the investigator for guidance. These questions are to determine whether the proposed exercise is appropriate for you. Your answers will be kept strictly confidential.

1.	You are.....	Male	Female
2.	What is your exact date of birth? Day..... Month.....Year..19..... So your age is..... Years		
3.	When did you last see your doctor? In the: Last week..... Last month..... Last six months..... Year..... More than a year.....		
4.	Are you currently taking any medication?	YES	NO
5.	Have you ever suffered from trauma or injuries to your neck, or back?	YES	NO
6.	Have you ever had asthma, or any other respiratory conditions?	YES	NO
7.	Have you had any abdominal or spinal surgery?	YES	NO
8.	Have you ever been told you have a scoliosis?	YES	NO
9.	Do you ever get neck or back pain?	YES	NO

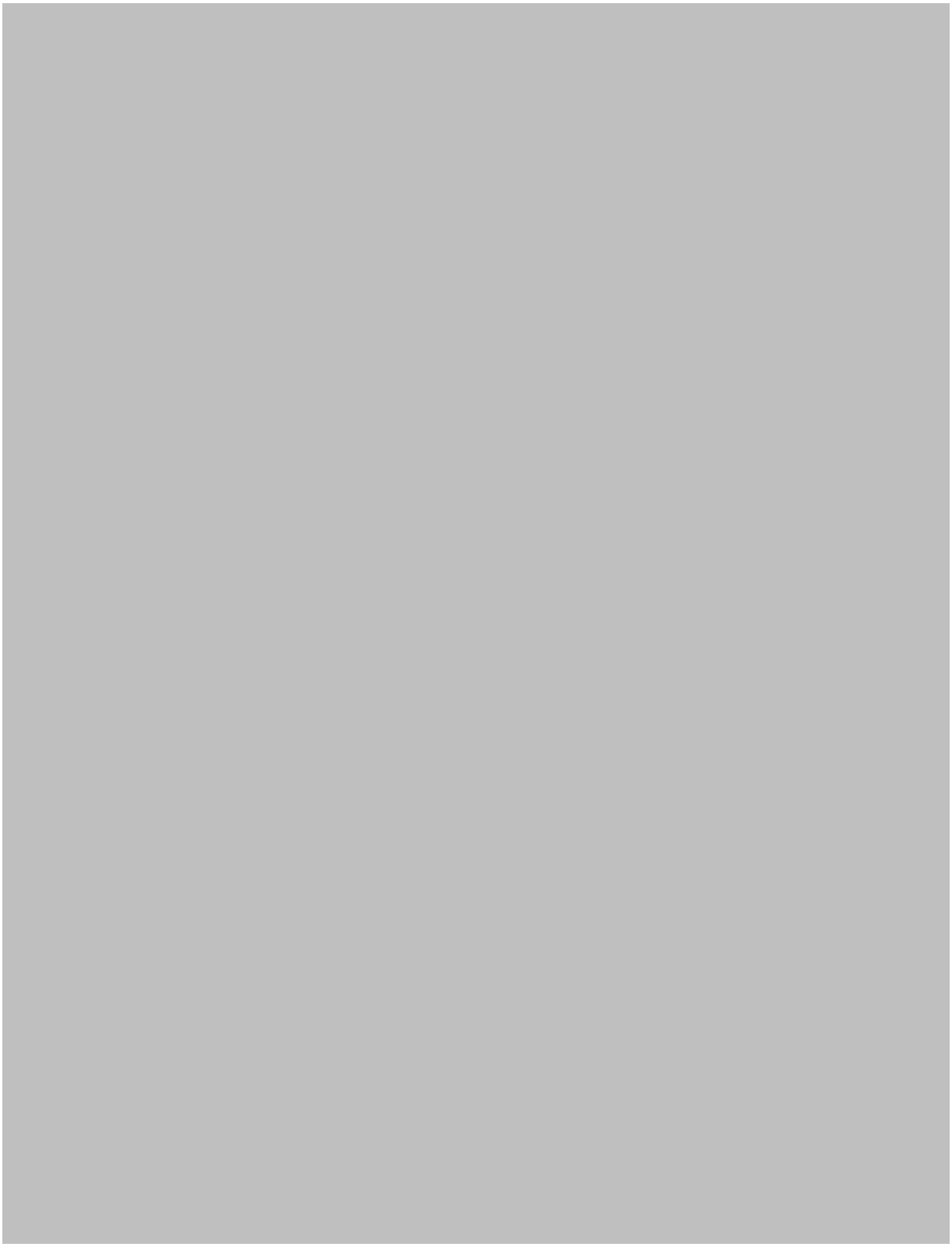
10.	Have you ever experienced your joints swelling up for no apparent reason?	YES	NO
11.	Have you ever seen a doctor or specialist for symptoms in your neck, back, joint or soft tissues	YES	NO
12.	Is there any family history of back or neck pain?	YES	NO
13.	Have you ever had viral hepatitis?	YES	NO
14.	If you are female, to your knowledge, are you pregnant?	YES	NO
15.	Have you ever been told you have hypermobility or loose joints?	YES	NO
16.	What is your current weight?		
17.	What is your current height?		
18.	What is your hand dominance?		

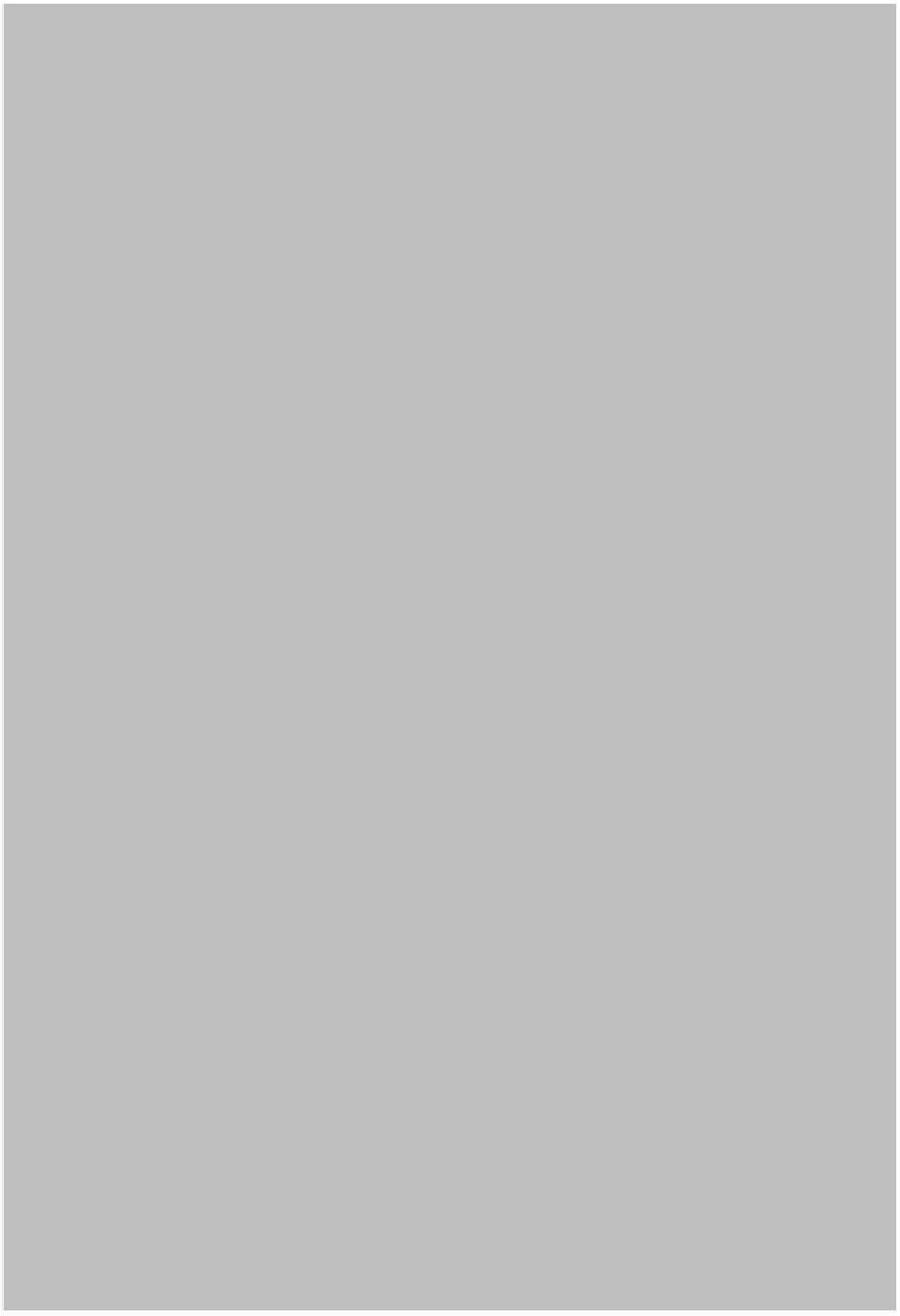
I have completed the questionnaire to the best of my knowledge and any questions I had have been answered to my full satisfaction.

Signed: .....

Date: .....

Appendix 15. Ethical approval





Appendix 16. Correlations

COPD group correlations for pulmonary function and additional measures

	FEV_1% predicted **Pearson's**	**FVC** **Pearson's**	**FEV_1/FVC** **Spearman's rho**
Thoracic spine rotation	-0.05	-0.08	-0.14
Cervical spine rotation	0.22	0.03	0.23
Cervical spine lateral flexion	0.11	-0.08	0.15
T8-C7 to vertical (degrees)	0.12	-0.01	0.21
C7-tragus to vertical (degrees)	-0.36*	-0.36	-0.23
Tragus-eye to vertical (degrees)	-0.05	0.00	0.00
Total PPT	0.12	-0.06	0.16
Bone mineral density	0.29	0.32	0.03
T score	0.26	0.37*	0.11
Hospital Anxiety and Depression Scale	-0.29	-0.24	-0.17
SGRQ total	-0.37*	-0.31	-0.23
Steroids			
Smoking pack years	0.21	0.02	0.14

- * significant at the level of 0.05 (2-tailed)
- ** significant at the level of 0.01 (2-tailed)

Control group correlations for pulmonary function and additional measures

	FEV_1% predicted	FVC	FEV_1/FVC
Thoracic spine rotation	0.16	0.24	0.06
Cervical spine rotation	-0.16	-0.23	0.01
Cervical spine lateral flexion	-0.03	-0.19	0.06
T8-C7 to vertical (degrees)	0.05	-0.17	0.36**
C7-tragus to vertical (degrees)	0.09	0.06	-0.09
Tragus-eye to vertical (degrees)	-0.08	-0.20	0.27
Total PPT	-0.28*	-0.26	-0.43
Bone mineral density	-0.21	-0.14	-0.13
T score	-0.18	-0.10	-0.12
Hospital Anxiety and Depression Scale	-0.22	-0.26	0.10
Smoking pack years	-0.12	0.01	-0.18

- * significant at the level of 0.05 (2-tailed)
- ** significant at the level of 0.01 (2-tailed)

Appendix 17.Sensitivity analysis for logistic regression

Medically supported diagnosis	Model 1 (minimally adjusted sex, BMI, age)		Model 2 (adjusted HADS)		Model 3 (adjusted smoking)	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Thoracic spine rotation	0.91 (0.87-0.95)	<0.001*	0.92 (0.88-0.97)	0.002*	0.90 (0.84-0.97)	0.003*
Cervical spine rotation	0.98 (0.96-1.00)	0.01*	0.98 (0.96-1.00)	0.12	0.98 (0.96-1.01)	0.23
Cervical spine lateral flexion	0.99 (0.97-1.01)	0.31	1.00 (0.97-1.02)	0.69	0.99 (0.96-1.02)	0.55
Muscle sensitivity	1.00 (1.00-1.00)	0.004*	1.00 (1.00-1.00)	0.06	1.00 (1.00-1.00)	0.27
Posture						
C7-tragus	1.05 (0.98-1.11)	0.15	1.05 (0.98-1.13)	0.16	1.15 (1.02-1.29)	0.02*
Thoracic spine posture	1.06 (0.96-1.15)	0.25	1.05 (0.94-1.17)	0.38	1.15 (0.98-1.35)	0.08
Tragus-eye	1.00 (0.95-1.07)	0.71	1.01 (0.94-1.08)	0.77	1.02 (0.93-1.11)	0.74
Spirometry based diagnosis	**Model 1 (minimally adjusted sex, BMI, age)**		**Model 2 (adjusted HADS)**		**Model 3 (adjusted smoking)**	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Thoracic spine rotation	0.93 (0.89-0.97)	<0.001*	0.94 (0.90-0.98)	0.006*	0.94 (0.90-0.99)	0.01*
Cervical spine rotation	0.98 (0.97-1.00)	0.07	0.99 (0.97-1.01)	0.32	0.99 (0.97-1.02)	0.56
Cervical spine lateral flexion	0.99 (0.97-1.01)	0.18	0.99 (0.97-1.01)	0.38	0.99 (0.96-1.01)	0.31
Muscle sensitivity	1.00 (1.00-1.00)	0.11	1.00 (1.00-1.00)	0.66	1.00 (1.00-1.00)	0.66
Posture						
C7-tragus	1.05 (0.99-1.12)	0.10	1.06 (0.99-1.13)	0.10	1.12 (1.02-1.22)	0.02*
Thoracic spine posture	1.00 (0.92-1.09)	0.99	0.98 (0.89-1.08)	0.70	1.00 (0.90-1.12)	0.99
Tragus-eye	1.00 (0.95-1.06)	0.90	1.00 (0.94-1.07)	0.99	1.00 (0.93-1.08)	0.96
OR; odds ratio,						