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Understanding the Role of Personal, Psychosocial and Occupational Factors and their Interactions on Low Back Pain Severity in Workers

Nirathi Keerthi Govindu

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By

Nirathi Keerthi Govindu

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By

Nirathi Keerthi Govindu

Approved:

Kari Babski-Reeves Associate Professor and Graduate Coordinator of Industrial and Systems Engineering (Director of Dissertation)	Daniel Peterson Professor of Biochemistry, Molecular Biology, Entomology and Plant Pathology (Minor Professor)
Burak Eksioglu Associate Professor of Industrial and Systems Engineering (Committee Member)	Lesley Strawderman Assistant Professor of Industrial and Systems Engineering (Committee Member)
Shane C. Burgess Committee Participant of Pathobiology/Population Medicine (Committee Member)	Sarah A. Rajala Dean of the College of Engineering

Name: Nirathi Keerthi Govindu

Date of Degree: May 10, 2013

Institution: Mississippi State University

Major Field: Industrial and Systems Engineering

Major Professor: Dr. Kari Babski-Reeves

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Candidate for Degree of Doctor of Philosophy

Low back pain (LBP) is the most prevalent work-related musculoskeletal disorder. Occupational risk factors have been studied for current ergonomic prevention strategies; however, other underlying mechanisms may exist since not all workers performing the same task develop the same severity. Previous research has identified personal and psychosocial risk factors that also contribute to LBP. Research quantifying the interactive effects of the various personal, psychosocial and occupational factors is limited, along with research on the effect of risk factor combinations on LBP severity.

The objectives of this study were to: 1) study the various factors that are known to be involved in low back pain and analyze interactions, and 2) develop a model to predict low back pain and validate it. In order to address these objectives, 2 studies were conducted.

The first study investigated the effects of various personal, genetic, occupational and psychosocial factors on two subjective LBP severity ratings: Oswestry Disability Index (ODI) and a Visual Analog Scale (VAS), and three physician-based ratings: MRI

severity, canal stenosis and nerve impingement. Personal and psychosocial factors, in addition to occupational factors, were found to significantly affect the severity ratings.

The second study involved building predictive models of LBP severity for each risk factor category as well as a combined risk factor model. Results showed that the combined risk factor models considering interaction effects both within and across risk factor categories were significantly better in predicting severity ratings than the individual models. However, validation conducted using 5 random samples showed inconsistent accuracies. Results obtained may help to develop a more reliable way to predict and, hence, prevent chronic LBP.

Keywords: Low back pain severity, personal factors, psychosocial factors, occupational factors

DEDICATION

I would like to dedicate this dissertation to my parents, Gopal Reddy and Parvathi Devi Govindu, and my husband Anup.

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CHAPTER I

INTRODUCTION

1.1 Background

Work related or occupational low back pain has become an issue of major concern in recent years with significant research conducted to identify causal risk factors and develop effective interventions. Low back pain is one of the most prevalent work-related musculoskeletal disorders (WMSD) with a reported 226,000 number of cases requiring days away from work in 2011 (BLS, 2012). WMSDs develop gradually, are difficult to control in the later stages and recur presents additional challenges. Low back pain is described as pain in the lumbosacral region of the spine (Garg & Moore, 1992).

Low back pain may be acute or chronic. Studies have shown that individuals with acute low back pain can be treated and recover within a month (Pengel, Herbert, Maher, & Refshauge, 2003), whereas chronic pain is harder to treat and may take longer to recover. Factors that are responsible for the transition of low back pain from an acute to chronic injury include individual, psychosocial and workplace factors (Fransen, et al., 2002). Therefore, a research emphasis is required for preventing the transition from acute to chronic back pain, as early identification of this transition could help prevent risks from persistent pain and disability (Shaw, Pransky, Patterson, & Winters, 2005).

Current ergonomic prevention strategies involve trying to minimize the impact of risk factors, especially occupational risk factors. However, it is believed that other

underlying causal mechanisms may exist since not all workers performing the same task develop an injury. Further research is required to develop a more reliable way to predict and prevent low back pain and injuries.

Research has identified different factors that are thought to be linked to low back pain. Three general classifications of risk factors for low back WMSDs have been identified: personal (associated with the individual predisposing them to the condition—e.g., age, gender, genetics, etc.), psychosocial (associated with organizational work practices—e.g., overtime, stress, etc.) and occupational (associated with the work task—e.g., repetition, force, etc.) factors. Besides the occupational factors involving lifting, bending, twisting etc.; personal factors such age, gender, genes, physical fitness, obesity (weight/BMI), smoking, alcohol consumption, medical and family history, as well as psychosocial factors such as job stress levels, type of job and job satisfaction have been identified as being associated with LBP (Garg & Moore, 1992; van Tulder, Koes, & Bombardier, 2002). Research findings are mixed for several personal risk factors, such as gender, body weight and alcohol consumption. For example, studies have illustrated that LBP development is equally likely for males and females, while others have shown that females generally report higher rates of LBP than males (Leboeuf-Yde, Nielsen, Kyvik, Fejer, & Hartvigsen, 2009). Other studies have shown that hormonal and reproductive factors may have a role in higher reported rates of LBP in women (Frymoyer, et al., 1983; Mogren, 2008; Wijnhoven, de Vet, Smit, & Picavet, 2006). Associations between body weight and LBP could not be established due to insufficient data (Leboeuf-Yde, 2000b), but an increased prevalence in LBP with increasing body mass index (BMI) has been reported (Orvieto, Rand, Lev, Wiener, & Nehama, 1994). Alcohol consumption

showed no relation to LBP, but it cannot be ignored as a factor unless further larger studies are conducted (Leboeuf-Yde, 2000a). Smoking was also not found to have a strong association with low back pain but studies exist that do show a relation (Leboeuf-Yde, 1999). Increasing age did not necessarily show higher LBP incidence rates (Leboeuf-Yde, et al., 2009), potentially due to older individuals transitioning outside of the working population for high risk jobs (Dionne, Dunn, & Croft, 2006).

Genes were also studied as risk factors for low back pain (Ala-Kokko, 2002; Manek & MacGregor, 2005). In general four genes; the collagen gene, the aggrecan gene, the interleukin 1 gene and the Vitamin D receptor gene; have been shown to be related to low back pain (Kawaguchi, et al., 1999; Paassilta, et al., 2001; Solovieva, et al., 2004; Videman & Battie, 1999). It is not known whether a single gene has a major effect on LBP or whether the condition is due to effects of several genes, though the latter idea is more likely (Kalichman & Hunter, 2008).

Psychosocial factors such as low job satisfaction, monotonous tasks, social relations, perceived demands, self-reported stress, and work pace, on the other hand, seem to show a strong association with low back pain (Hoogendoorn, van Poppel, Bongers, Koes, & Bouter, 2000; Linton, 2001). Though psychosocial factors may not be an actual cause of low back pain, studies show that it could lead to chronicity (Gatchel, Polatin, & Mayer, 1995).

From the literature available it is evident each factor can contribute to LBP in and of themselves, but these factors are not mutually exclusive and interaction effects also need to be studied to fully explain the incidence of low back pain (Marras, 2005). Further research is required to study interactions of the various personal, psychosocial and

occupational factors and their effects on low back pain in order to identify a combination of factors that may increase injury risk and also to address the question of why some workers are at a higher risk of injury than others doing the same task.

1.2 Objectives

The long term goal of this research is to develop a predictive model of LBP that is inclusive of multiple risk factors. Considering risk factors from multiple categories and their interactions could help describe why some individuals are more susceptible to LBP development. The objective of the research was to study various factors that are known to be involved in low back pain, analyze their interactions, develop a model to predict low back pain and validate it. Once the model predicting low back pain has been validated, extending this to other WMSDs would follow.

1.3 Research Outline

The main objective of the study was to identify factors involved in occupational low back pain and to develop a predictive LBP model. The dissertation work studied various personal (age, gender, obesity, genes, physical activity level, alcohol and smoking), psychosocial (perceived stress and job stress) and occupational factors that have been found to contribute to low back pain.

Literature Review: A literature review was conducted to learn more about the different factors that were found to be involved in low back pain. It also helped in developing suitable methods for the study.

Study 1: The first study involved data collection from a participant population already suffering from LBP. A demographic questionnaire was used to obtain personal

information. Gene information was obtained by analyzing and/or sequencing the 4 genes to look for polymorphisms that may be responsible for LBP. A perceived stress questionnaire and a Job Content Questionnaire (JCQ) were used to collect psychosocial related information. Questions from the demographic questionnaire were used as occupational factors. Low back pain intensities were obtained through MRI interpretations (objective) as well as pain questionnaires (subjective) completed by the participants. The cumulative gene effects were also measured using the pain questionnaires as well as genetic data. This was done by comparing the reported incidents and severity of the low back pain with the extent of the involvement of each gene.

Hypotheses:

1. Presence of the factors being studied contributes to low back pain in workers.

    a. Personal factors will significantly affect both subjective and objective LBP severity ratings.

    b. High smoking levels and alcohol consumption; as well as low physical activity levels will correspond to high severity ratings.

    c. (i) Polymorphisms present in the 4 genes being studied will significantly affect objective LBP severity ratings. (ii) Polymorphisms may be only present in those with LBP. (iii) Presence of polymorphisms in more than 1 gene will correspond to higher severity ratings.

    d. Perceived stress and job stress will significantly affect subjective LBP severity ratings with higher stress corresponding to higher ratings.

    e. Occupational factors will significantly affect both subjective and objective LBP severity ratings.

2. Interactions within and between risk factor categories will significantly affect severity of LBP.

3. MRI interpretations and self-assessed pain questionnaire scores will be correlated.

Study 2: Regression models were developed for each factor and risk factor interactions to identify the best predictors of low back pain. A final model to predict the risk of low back pain was developed and validated.

Hypothesis:

1. Presence of several of these factors increases the risk of low back pain in workers.
2. Interaction of factors will significantly affect severity of LBP.

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CHAPTER II

STUDY 1: DETERMINING THE EFFECTS OF PERSONAL, PSYCHOSOCIAL AND OCCUPATIONAL FACTORS IN THE ASSESSMENT OF LOW BACK PAIN

2.1 Introduction

Occupational injuries and disorder prevalence has been a major issue of concern for the past few decades. Worker absenteeism and costs associated with the treatment and compensation of workers with low back pain and other work-related musculoskeletal disorders (WMSDs) have increased, resulting in this increased concern. WMSDs accounted for 33% of injuries involving days away from work in 2011 (BLS, 2012). Low back pain (LBP) is the most prevalent WMSD and has received significant attention by researchers in an attempt to predict and prevent LBP in workers.

Initial research pointed towards physical damage to the spine as the most important factor dictating LBP, but current research on spinal damage as a factor has presented controversial results. This led to investigations of other possible causal factors, such as psychological, physiological, genetic, biomechanical, etc. Research on each of these factors has shown some degree of association with LBP. However, most studies have explored each factor in isolation from the others. Studying risk factor effects in isolation of other effects fails to quantify interactive effects of risk factors on LBP (Marras, 2005).

A conceptual model designed by Marras (2005) (see figure 2.1) illustrates how different factors contribute to LBP both by themselves and through interactions with other factors. Research is conducted to test for interrelationships between risk factor categories have demonstrated the need for continued research in this area (Marras, 2005). Several broad categories of risk factors for LBP have been studied and include personal, genetic, physiologic, psychosocial and biomechanical factors. These factors are thought to be most likely multidimensional, complex and interactive (Marras, Ferguson, Burr, Schabo, & Maronitis, 2007). For example, the genetically determined, personal factors that lead to 'natural progression' of disc degeneration is probably modified to some degree by environmental factors such as lifting heavy weights (Battie, Videman, & Parent, 2004).

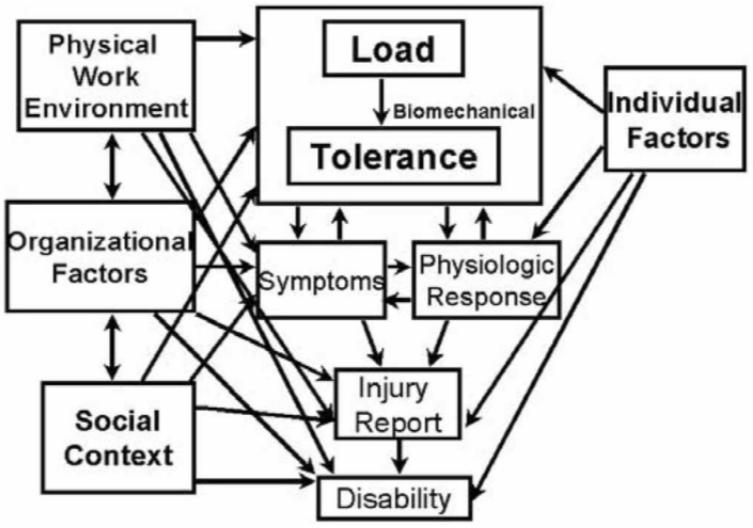

Figure 2.1 Conceptual model of how factors affect low back responses (Marras, 2005)

For occupationally induced low back pain, understanding how other factors (e.g., personal or genetic factors) may have contributed to LBP is critical in mitigating injuries. Also, since WMSDs are difficult to diagnose in early stages, early identification of risk would be beneficial. Therefore, the objective of this study was to identify factors and interactions that contribute to LBP severity and to quantify them. The factors identified here were then used to develop a predictive model for LBP severity.

2.2 Literature Review

2.2.1 Musculoskeletal Disorders and the Low Back

The vertebral column consists of an articular triad that forms its basic anatomical and functional unit. The articular triad is composed of the fibrous intervertebral joint and the two synovial vertebral joints. The triad is stabilized by a ligamentous apparatus and spine movements are possible by the action of complex muscle function coordination and gravity. The fibrous intervertebral joint consists of two intervertebral bodies and the intervertebral disc. The disc in turn is composed of the nucleus pulposus and annulus fibrosus. The annulus fibrosus mainly consists of collagen fibers. Small amounts of collagen are also found in the nucleus pulposus. Proteoglycans, especially aggrecan, are a major component of the nucleus pulposus. Collagens provide tensile support for the disc and proteoglycans provide tissue resistance to compressive forces on the spine (Ala-Kokko, 2002). When the spine is flexed or extended, bilateral sliding movements in the lumbar articular processes and displacement of the nucleus pulposus takes place. Sliding movements in the vertebral joints are also responsible for lateral bending of the spine (Hirsch, Ingelmark, & Miller, 1963).

One main source of low back pain that was accepted widely years ago was the degenerative changes in the lumbar discs (Hirsch, et al., 1963). The pathology of LBP is still not fully known, though some possibilities suggested are anular ruptures, irritation of nerve roots due to mechanical entrapment, immunologic reactions from exposure to substances from the nucleus pulposus and neuropathic changes. Loss of water content in the nucleus pulposus and anular tears are involved in early degenerative changes and are commonly associated with endplate irregularities and disc herniation (Videman & Battie, 1999). The low back is subjected to loads, torsion, flexion, and extension and the effect on the anatomical structures may be significant. The effects of these forces on structures; such as muscles, tendons, ligaments, and joints; could lead to poor postural control and altered kinematics that facilitate LBP (Bhandary, Chimes, & Malanga, 2010).

A specific diagnosis for LBP is complicated because almost all lumbar abnormalities are possible sources of pain (Kjaer, Leboeuf-Yde, Korsholm, Sorensen, & Bendix, 2005). LBP is thought to be multifactorial with many possible etiologies. LBP is a symptom that a person reports and cannot be validated by an external standard. Therefore, epidemiology of LBP is not clear. Studying the epidemiology can help in identification of risk factors by providing a link between pain and risk factor exposures. LBP is considered acute if discomfort persists 6 weeks or less and chronic if pain lasts longer than 12 weeks. The upper body is supported by the lumbar spine by transmitting forces and maintaining mechanical stability which is an energetically costly process. During physical work, changes in postures and loads may result in the sudden need for the spine to regain stability which may consequently result in excessive muscle activity

and tissue overload. When such activities are prolonged, e.g., increasing the load to maintain stability, they may lead to chronic LBP (Cholewicki & McGill, 1996)

2.2.2 Factors Contributing to Low Back Pain

In industry, back pain is referred to as 'back injury'. This implies that back pain is caused due to work-related factors only. Although, the amount heavy lifting present in occupations has declined in the recent years, LBP reporting has not (Videman & Battie, 1999). Therefore, it is evident that the onset of low back pain (LBP) could be due to various reasons (Table 2.1) Several risk factors have been identified and further research is being conducted to prove causation (Manchikanti, 2000). Few studies indicate that a history of LBP could be a predictor of serious LBP in the future. Other studies suggest that morphology of the intervertebral disc establishes the presence and severity of LBP, while still others point towards psychosocial factors as a cause for disabling LBP. A study concluded that psychological factors may not be important in the incidence of LBP and may be a consequence rather than a cause of occurrence (Roland & Morris, 1983). Yet another study found that persistence of symptoms was associated with low physical activity, smoking and job dissatisfaction (Thomas et al., 1999).

Table 2.1 Potential risk factors for LBP

Category	Risk Factors			
Personal	Age Genetics	Gender Smoking	BMI Alcohol	Family history Physical activity
Psychosocial	Perceived stress Decision latitude	Job stress Job security	Job satisfaction Job demands	Social relations Organizational level
Occupational	Physical load Bending	Force Twisting	Repetition Lifting	Vibration Posture

Recent studies have found that the relation between abnormalities in the lumbar spine and LBP is controversial. A study by Jensen et al. (1994) on individuals with no LBP showed that a large percent of the subjects had an abnormality of the spine as seen on the MRI (Table 2.2). Based on this, it has been suggested that the presence of an abnormality, such as a bulge or protrusion, in the lumbar region of a patient with LBP may be coincidental although the prevalence of extrusions in people with symptoms of LBP was found to be higher than in people without symptoms (Jensen et al., 1994).

Table 2.2 Abnormalities of lumbar spine in asymptomatic individuals (Jensen, et al., 1994)

Intervertebral Disk Abnormalities		**Non-intervertebral Disk Abnormalities**	
Normal	6%	Schmorl's nodes (herniation of the disk into the vertebral-body end plate)	9%
Bulge (circumferential symmetric extension of the disk beyond the interspace)	52%	Annular defects (disruption of the outer fibrous ring of the disk)	14%
Protrusion (focal or asymmetric extension of the disk beyond the interspace)	27%	Facet arthropathy (degenerative disease of the posterior articular processes of the vertebrae)	8%
Extrusion (more extreme extension of the disk beyond the interspace)	1%		

Even though degeneration of the disc was only moderately associated with LBP, modic changes (MC), were found to be strongly associated with LBP. MC, described by (Modic, Masaryk, Ross, & Carter, 1988) for the detection of anomalies, is defined as "signal changes in the vertebral bone extending from the vertebral end plate by MRI". It has been suggested that MCs are a possible later stage/step of disc degeneration. In a study, it was found that people with both disc degeneration and MC reported LBP more than those with just disc degeneration (Kjaer, Korsholm, Bendix, Sorensen, & Leboeuf-Yde, 2006).

2.2.2.2 Personal Factors

2.2.2.2.1 Age and LBP

Increasing age has been associated with LBP in some studies but age has still not been established as a risk factor because several studies have seen decreases in LBP reporting rates in the older population. It is a well known fact that the intervertebral discs undergo degenerative changes as age increases (Buckwalter, 1995). The percentage of subjects with degenerated disks increased with age in a study and the increase was more rapid in subjects with LBP (Paajanen, Erkintalo, Parkkola, Salminen, & Kormano, 1997). What is not understood is why decreases in LBP in the older population are seen. Some possible explanations given are cognitive impairment, depression, decreased pain perception and increased tolerance to pain. It is also possible that the elderly are under-represented in the back pain literature. A suggestion is that LBP usually begins in early life and has its highest frequency around the working age of 35-55 years (Leboeuf-Yde, Nielsen, Kyvik, Fejer, & Hartvigsen, 2009). However, duration of symptoms increased with age after this age and the pain lasted longer (Manchikanti, 2000). A literature review considering studies dealing with only severe forms of back pain found an increase in prevalence with increasing age (Dionne, Dunn, & Croft, 2006). Since aging has known effects on the bones and muscles, the older population is at a higher risk of LBP and therefore, age is considered a risk factor for LBP.

2.2.2.2.2 Gender and LBP

The effects of gender on LBP are yet to be confirmed, but it is a common observation that women are more likely than men to report LBP and also more likely to have pain for longer periods (Leboeuf-Yde, et al., 2009). Several epidemiological

investigations were conducted and only small gender differences were reported in many of them. Reasons for women to be more prone to LBP have been linked to menstruation, pregnancy, and labor. Use of oral contraceptives has also been associated with incidences of LBP (Wreje, Isacsson, & Aberg, 1997). Back pain during pregnancy is usually attributed to increased biomechanical strain or an altered hormonal influence (Manchikanti, 2000; Wijnhoven, de Vet, Smit, & Picavet, 2006; Wreje, Isacsson, & Aberg, 1997). Though, there are several reasons for women to develop LBP, higher incidences of LBP are reported in women performing physically demanding jobs (Garg and Moore, 1992).

2.2.2.2.3 Obesity and LBP

A literature review found that 32% of all the studies considered reported statistically significant positive, but weak, associations between weight and LBP, suggesting that obesity may not be a causal factor of LBP (Leboeuf-Yde, 2000b). One study found a strong association of Body Mass Index (BMI) with LBP where an increased prevalence was observed with increasing BMI (Orvieto, Rand, Lev, Wiener, & Nehama, 1994). The authors suggest that similar studies where weight was used as a measure of obesity and failed to show any association since weight alone is not considered a true index of obesity. Several biological reasons are put forward as possible explanations as to how obesity can influence LBP. First, the additional weight may generate higher mechanical stresses and loads on the spine (Orvieto et al., 1994). Second, the presence of fatty tissue decreases blood flow and vital nutrients required for healing leading to increased LBP. Third, obesity leads to loss of endurance. Obesity in relation to herniated lumbar intervertebral discs also showed interesting results. One study

concluded that intervertebral disc-herniation symptoms were more common in women who were overweight or who had a larger waist circumference (Han, Schouten, Lean, & Seidell, 1997). Other studies have also found significant correlations between body mass and disc herniation (Manchikanti, 2000). Therefore, although higher body masses may not be linked directly to LBP, obesity may be a marker or confounder for some other factor which is the actual cause of severe LBP (Leboeuf-Yde, 2000b).

2.2.2.2.4 Smoking and LBP

A literature review of smoking effects on LBP found inconsistent results (Leboeuf-Yde, 1999). Roughly half of the studies including smoking reported associations, though these were weak and were seen only in large samples. There was also a tendency of ex-smokers to have less LBP than current smokers. However, *Frymoyer* et al. (1983) found that individuals with severe LBP were more likely to be smokers than non-smokers. Several mechanisms by which smoking affects LBP are suggested. Significant correlations were found between smoking and intervertebral disc degeneration. Smoking affects the circulatory system outside the disc which in turn affects cellular update and metabolic production within the disc (Holm & Nachemson, 1988). Additionally, intraspinal pressure due to repeated coughing may lead to LBP (Gyntelberg, 1974). A study noted breathing ability differences while handing loads may contribute to LBP as the muscles used for breathing are also used to maintain the spine. Therefore, smokers and others whose lung elasticity has been weakened may be at risk of LBP (McGill, Sharratt, & Seguin, 1995).

2.2.2.2.5 Alcohol Consumption and LBP

In a literature review, it was reported that none of the studies reported a positive association between LBP and alcohol consumption, but emphasized that further studies are needed to fully ascertain that alcohol consumption does not play any role in LBP due to lack of 'well designed alcohol-LBP-centered studies' (Leboeuf-Yde, 2000a). Establishing a link between alcohol consumption on LBP is complicated as the use of self-reports may not be accurate due to the possibility of under reporting. Alcohol consumption may contribute to LBP by inducing uncoordinated movements altering biomechanical loads on the spinal structures. Further, alcohol consumption has been associated with psychosocial problems which are thought to contribute to LBP and chronicity.

2.2.2.2.6 Physical Activity and LBP

The association of physical activity to LBP is not well understood. Several studies have reported a higher incidence of LBP and disc herniation in populations that exercised regularly, but others reported the opposite results (Manchikanti, 2000). It is not clear whether regular physical activity could increase or decrease the risk of LBP though many believe it can help reduce symptoms. Regular physical activity could prevent disc degenerations by an adaptive increase in annular and ligamentous strength (Porter, 1987). It is also commonly believed that inactivity and lack of exercise could lead to an increase in LBP and disability and a good fitness level could help with faster recovery. Another theory suggested was that certain types of physical activity that are performed to increase endurance may lead to the transport of small solutes in and out of the disc, thus increasing nutrition and making the back stronger (Porter, 1987; Sward, et al., 1991).

Extreme sports, on the other hand were associated with greater disc degeneration (Videman, et al., 1995). Therefore, regular physical activity to maintain general physical fitness may help reduce the severity of LBP, though activities that put unusual loads on the spine may have the reverse effects.

2.2.2.2.7 Genetics and LBP

Battié et al (1995) stated that "disc degeneration may be explained primarily by genetic influences and by unidentified factors, which may include complex, unpredictable interactions" (Battie, et al., 1995). The mechanism through which genetic factors could lead to disc degeneration can be explained by its influence on the mechanical properties of the spine that may change its shape and size, thus making it vulnerable to external forces. Another mechanism is through biological processes, such as the synthesis and breakdown of the disc's structural and biochemical constituents, which is also controlled by genetic factors, and, if altered, could lead to faster and unnecessary changes that may lead to LBP (Battie & Videman, 2006). Though these are likely explanations, it should be understood that disc degeneration is only one mechanism through which genes influence LBP (Battie, Videman, Levalahti, Gill, & Kaprio, 2007).

A review of the literature identified that the following genes are being investigated with respect to LBP: the aggrecan gene, the matrix metalloproteinase-3 gene, the vitamin D receptor gene, and the interleukin-1 gene (Ala-Kokko, 2002, Chan, et al., 2006). Three of these genes are structural genes and one is a gene that is involved in inflammatory responses. As stated previously under section 2.2.2, many studies have argued that structural changes to the spine is the factor that leads to severe back pain but

other studies have shown that there is little correlation between disc degeneration and low back pain. Therefore, both types of genes are being studied to investigate the role of each.

Collagen IX (COL9) gene: The gene codes for collagen IX that forms the extracellular matrix present in the cartilage as well as the nucleus pulposus of the intervertebral disc and, therefore, is a good candidate to study as changes in the gene sequence directly affect the constitution of the intervertebral disc (Cha et al., 2006). Studies on the COL9A2 and COL9A3 genes, that code for the α2 and α3 chains of collagen IX, identified sequence variations that were associated with disc degeneration (Annunen, et al., 1999; Paassilta, et al., 2001). In particular, a gene substitution that leads to an amino acid change to tryptophan (trp2 and trp 3 alleles) were studied. Some studies showed higher associations of the COL9A3 gene to disc degeneration than the COL9A2 (Kales, et al., 2004; Solovieva, et al., 2006). For this reason, the COL9A3 gene has been chosen for this study. The mechanism of how the products of the trp 2 and trp 3 alleles act as risk factors is not clear since the function of collagen IX in the cartilage is still not known (Chan, et al., 2006). Since collagen is a major component of the extracellular matrix, polymorphisms may lead to defective proteins that may alter the mechanical properties of the intervertebral discs making it prone to herniation and LBP (Tegeder, 2009).

Interleukin 1 (IL-1) gene: The gene codes for a cytokine, interleukin-1, which is produced in response to infection/injury and elicits a neurological response. It has been identified that high levels of these inflammatory substances could be responsible for greater pain responses and, therefore, is a good candidate to be studied. The IL-1 gene family consists of IL-1α, IL-1β (both strong inducers of inflammation) and IL-1RN that

modulates the effect acting as a receptor antagonist (Chan, et al., 2006; Solovieva, et al., 2004). It was found that carriers of the IL-1RN gene had an increased risk of LBP and this gene in combination with IL-1α and IL-1β had a higher risk (Solovieva, et al., 2004). Therefore, the IL-1RNA^{1812} region of the gene has been chosen to be studied. It is suspected that polymorphisms lead to a defective IL-1RN that fails to modulate the pain responses leading to greater pain perceptions in the back.

Vitamin-D Receptor (VDR) gene: The VDR gene codes for the receptor for vitamin D3 and has a role in bone mineralization (Chan, et al., 2006). Abnormalities could lead to bone weakening which could be responsible for LBP. Further, VDR expression was also studied in cartilage and proteoglycan synthesis, both of which are present in the intervertebral disc. Therefore, this gene has been chosen. Studies have shown that 2 intragenic polymorphisms of the VDR gene (called Taq and Fok polymorphisms present in exon 2 and exon 9 respectively) are associated with disc degeneration (Videman, et al., 1998). The mechanism of how the Taq polymorphism affects is not clear. The Fok polymorphism eliminates the first ATG translation initiation codon and allows the second codon to be translated, leading to proteins on different lengths (Chan, et al., 2006).

Aggrecan (AGC1) gene: The gene codes for aggrecan, a major proteoglycan component of the intervertebral disc. Aggrecan is present both in the cartilage and the nucleus pulposus. Exon 12 of AGC1 codes for half of the keratin sulphate (KS) binding domain and the entire chondroitin sulphate (CS) binding region. Its main function is to maintain the hydration of the disc structure through the CS chains. Abnormalities in this protein can have a direct impact on LBP making it a good candidate to study (Chan, et

al., 2006). Studies have shown the association of Aggrecan gene variable number tandem repeats (VNTR) with disc degeneration (Kawaguchi, et al., 1999; Solovieva, et al., 2007). Therefore, the aggrecan gene VNTR region was chosen to be analyzed. These repeat regions differed in individuals and Kawaguchi (1999) found that small number of repeats were associated with disc degeneration, likely due to fewer CS chains and, therefore, poorer disc hydration leading to degeneration (Ala-Kokko, 2002). In the human AGC1 gene, VNTRs are present ranging from 13 to 33 repeats.

In addition to the contribution of each gene individually, gene-gene interactions and gene-environment interactions may exist that need to be investigated. Evidence exists that body weight modifies the effect of COL9A3 on LDD. Further, associations between collagen and interleukin gene cluster polymorphisms and LDD have been reported (Kalichman & Hunter, 2008). Therefore, those with shorter repeat alleles for the AGC1 gene, presence of the taq or fok polymorphism in the VDR gene, and presence of the single nucleotide polymorphism (SNP) in the COL9A3 and Il-1RN genes have a higher risk of LBP, and these polymorphisms present together or in presence of other risk factors may further increase the risk.

Several personal factors such as age, gender, obesity, physical activity level, smoking, alcohol consumption and genetics are thought to be risk factors of LBP. Personal factors are important to study as risk factors for occupational LBP as they explain the inherent variability between workers who are subjected to the same set of occupational risk factors. Further, although the job factors may be altered or changed to reduce risk, some personal factors; such as age, genetics etc.; cannot be controlled. These

factors are expected to contribute to the severity of LBP by itself and in combination with the other risk factors.

2.2.2.3 Occupational Factors

MSDs in the workplace have been studied extensively and it is a common notion that the work itself is a major cause of MSDs (Wind et al., 2005). Occupations that involve heavy physical work, vibration and awkward postures probably lead to disc degeneration and LBP. Exposure to these factors cannot be quantified easily and the relationship of occupational factors with LBP is difficult to comprehend (Manchikanti, 2000). One explanation is that these mechanical factors cause damages to the spine through a single incident or repeated loading. Though occupational factors have been associated with degeneration, the variability explained by them is very small (Videman & Battie, 1999).

2.2.2.3.1 Heavy Physical Work and LBP

Work involving large forces and loads have been strongly associated with the occurrence of LBP (Manchikanti, 2000). It was also observed that individuals with back pain were involved in heavy work which was thought to be associated with symptoms (Carragee, Alamin, Miller, & Carragee, 2005). In a survey study of men between ages 18 to 55, out of all the occupational factors studied, heavy lifting was found to be the most strongly associated with LBP (Frymoyer, et al., 1983). Therefore, workers with high force requirements or the need to lift heavy loads are at a higher risk of LBP and the amount of force required/ load lifted is considered an important risk factor.

2.2.2.3.2 Work Postures, Bending, Twisting and Lifting, and LBP

It is known that muscle activity is required even to maintain an upright posture. This muscle activity is less as long as the body segments are well aligned with respect to the center of gravity. When the trunk is bent, there is a shift in the center of gravity. In order to maintain equilibrium, counterbalancing muscle forces are required which can be quite high. These forces act on the spine and must be balanced by the spinal muscles (Pope, Goh, & Magnusson, 2002). Frequent bending and twisting in jobs has been thought to be a cause of back injuries. Lifting in addition to bending and twisting was found to be even more harmful. It was observed that the incidence of LBP in workers who performed heavy manual lifting was 8 times greater than workers with sedentary jobs (Manchikanti, 2000). An explanation for how bending can be harmful is that while bending, muscles are no longer active and only the soft tissues play a role. These types of tasks generate loads on the spine that exceed failure loads. In the aged workers, this further enhances their risk of injury (Pope, et al., 2002). Asymmetrical lifting is considered a strong risk factor for LBP as small deviations from the sagittal plane when lifting can increase the risk (Kingma et al., 1998). In addition to trunk postures, it was found that jobs that required sitting for prolonged periods were also at an increased risk of LBP. Studies also reported that people who had jobs that required them to drive for more than half their work day had an increased risk of disc herniation due to combined effects of sitting and vibration (Manchikanti, 2000). Therefore, although heavy physical work and loads lifted are considered the major risk factors for LBP, work postures are also important to be studied since factors such as asymmetrical lifting, and prolonged sitting and standing have also been associated with LBP.

2.2.2.3.3 Vibration and LBP

Whole body vibration has been associated with LBP, although no sufficient evidence exists for an exposure-response relationship between vibration and LBP (Manchikanti, 2000). Vibration is also studied as a risk factor for intervertebral disc disease. A study demonstrated that automobile driving was more frequent in those with LBP than those without, further suggesting the possible link between whole body vibration and LBP (Frymoyer, et al., 1983). Recent studies have also shown that vibration has an additive effect with genetic risk factors (Virtanen, et al., 2007). Therefore, workers who are subjected to whole body vibration in addition to other risk factors are at a risk of developing severe LBP.

Occupational factors are considered important risk factors for LBP as these factors directly impose strain on the spine leading to LBP and are linked to incidence of LBP, severity and disability. Factors such as high amounts of load lifted, presence of bending, twisting, and vibration on the job are thought to increase the risk of LBP on workers. However, workplace factors alone may not be responsible since workers with sedentary jobs also develop LBP.

2.2.2.4 Psychosocial Factors

Since occupational factors alone failed to explain the causality of LBP, biopsychosocial models were developed to explain the occurrence of LBP since it was found that both physical and psychosocial factors were associated with the onset of LBP (Feyer, et al., 2000; Pincus, Burton, Vogel, & Field, 2002). Several possible mechanisms by which psychosocial factors can lead to LBP can be explained. Presence of psychosocial factors may influence changes in posture, movement and forces exerted

which may impact biomechanical load. For example, Marras (2000) found that if a worker is under psychosocial stress while performing a lifting task, it leads to increased muscle activity and increased spine compression and lateral shear (Marras, 2000). These factors can also elicit certain physiologic mechanisms, such as increased muscle tension or hormonal excretion, which may influence pain perception. Presence of these factors may also affect the ability of an individual to cope with pain and also influence reporting of symptoms (Hoogendoorn, van Poppel, Bongers, Koes, & Bouter, 2000).

Psychosocial factors thought to affect LBP include worker satisfaction, attitudes towards employers, quality of interactions between workers and supervisors, monotony at work, etc. (Manchikanti, 2000). Strong evidence between job satisfaction, monotonous tasks, work relations, demands/load, perceived stress, decision latitude and perceived ability to work were found for future back pain problems. There was only moderate evidence established for work pace, control, emotional effort at work, and the belief that work is dangerous, and inconclusive evidence about work content (Hoogendoorn, et al., 2000; Linton, 2001).

Psychosocial factors have also been associated with influencing the development of chronicity of LBP (Slater, et al., 2009). A literature review conducted on psychological factors as risk factors for back pain concluded that psychological factors were associated with both acute and chronic pain particularly in the transition from acute to chronic symptoms (Linton, 2000). These factors are thought to have a greater impact on disability than biomechanical factors and, hence, can be used as predictors for chronic LBP (Gatchel, Polatin, & Mayer, 1995; Linton, 2000; Pincus, et al., 2002). A study suggested that understanding psychological problems early is vital in preventing the progression

into chronicity (Burton, Tillotson, Main, & Hollis, 1995). Studying these factors, therefore, can increase the opportunity of initiating early preventive measures.

2.2.2.4.1 Job Content Questionnaire (JCQ)

Self-report questionnaires are used by researchers to measure subjective estimates of exposure to psychosocial factors due to the ease of administration, lower cost and time requirements. It was also found that self-reports are strongly correlated with objective ratings of the workplace obtained through observations of the work environment (Benavides, Benach, & Muntaner, 2002). Several questionnaires have been designed and validated to quantify psychosocial factors. Of these, the Job Content Questionnaire (JCQ) is one of the most commonly used. It consists of the following sections: psychological demands, decision latitude, social support, physical demands, job insecurity, job satisfaction and organizational level (Karasek, et al., 1998). The recommended version consists of 49 questions where most items are rated using a 4-point Likert scale. The decision latitude section is further divided into skill discretion and decision authority. Psychological demands refer to the mental workload. Social support deals with relationships with both coworkers and supervisor.

2.2.3 Low Back Pain Measures – Objective and Subjective Severity Scales

2.2.3.1 Magnetic Resonance Imaging (MRI)

Magnetic resonance imaging (MRI) has proven to be effective in faster and more definite diagnoses of conditions in patients even at early stages. In the case of LBP, the use of MRI is for the detection of disc hernitaions in order to assess whether surgical intervention is necessary. Using MRI scans, reduced signal intensity, irregularities of

nucleus's shape, reduced disc height, anular tears, changes in disc contour (bulges, protrusion, extrusion etc), endplate irregularities and Modic type changes can be detected (Kjaer, et al., 2005). A problem with using MRI interpretations for LBP severity is that disc herniations, disc bulges and disc degenerations are also observed in people with no pain in the lumbar region (Jarvik, et al., 2003). Few studies exist that report associations between disc pathology and LBP (Beattie, Meyers, Stratford, Millard, & Hollenberg, 2000; Boos, et al., 1997). However, the strongest associations were found for lifetime pain and not for current pain status (Videman, et al., 2003). In this study, MRI interpretations will be collected for the patients as an objective measure of severity. Since the population consists of patients with LBP, using this measure may not be problematic. Further, correlation of these measures with subjective measures of pain severity during the patient's lifetime will also be analyzed.

2.2.3.2 Modified Oswestry Low Back Pain Disability Index

The Modified Oswestry Low Back Pain Disability Index (see Appendix F) was used as the subjective severity scale. The scale was developed to obtain an index of pain severity and disability in patients (Fairbank & Pynsent, 2000). Self-reported measures from questionnaires are usually used as outcome measures of pain and serves as a common language for researchers and clinicians. A good questionnaire consists of the following characteristics: responsiveness, factor structure, validity, reliability, should be economical, practical/feasible and easily administered (Cleland, Gillani, Bienen, & Sadosky, 2011; Fritz & Irrgang, 2001; Khorsan, Coulter, Hawk, & Choate, 2008). The Oswestry Disability Index (ODI) is one of the most widely used questionnaires and is one of the most validated outcome measures with respect to responsiveness. The ODI is a 10

item questionnaire with a 6-point ordinal scale that is used to assess back pain, both acute and chronic (Grotle, Brox, & Vollestad, 2004). It can also be used to evaluate function and disability as well as interference with several physical activities (Cleland, et al., 2011; Fairbank, 2000). The ODI has been shown to have good validity, reliability, responsiveness and can be self-administered in 5 minutes (Khorsan, et al., 2008). A modified version of the ODI is now being used that has high levels of both validity and reliability (for test-retest reliability and ICC of 0.9) (Fritz & Irrgang, 2001; Wind, Gouttebarge, Kuijer, & Frings-Dresen, 2005).

Scoring is done by adding the individual question scores, dividing the total by the total possible score and then multiplying by 100 to yield a percentage score (Maughan & Lewis, 2010). Since the final score obtained is a percentage that is a continuous variable, it is can be easily analyzed statistically. Further, it has been found that subjective measures now have the same reliability as objective measures (Khorsan, et al., 2008) and that ODI has also been correlated with pain intensity ratings (Gronblad, et al., 1993).

2.2.3.3 Visual Analog Scale (VAS)

Simple pain rating scales are very helpful for patients to rate pain intensity. The Visual Analog Scale (VAS), usually a 1cm long horizontal line with anchors at the ends, is one of the most common ways by which general pain intensities, both acute and chronic, are assessed (Khorsan, et al., 2008). This method has good validity, reliability, responsiveness and can be self administered in less than a minute. It was also found that pain severity ratings obtained from VAS and ODI had significant moderate correlations with a Pearson correlation coefficient of 0.62 (Gronblad, et al., 1993). Estimates of pain

severity can be obtained fairly quickly from the VAS but an immediate result may not be possible, since the scale has to be measured (Khorsan, et al., 2008).

2.2.4 Summary

LBP continues to be a prevalent condition in workers and techniques to predict and prevent severe and disabling LBP is required. Previous research has identified several risk factors for LBP, though few studies have investigated the impact of risk factor interactions on LBP severity. Further, though studies have identified that gene polymorphisms have been identified that are associated with LBP, no studies have included these in predictive models of LBP. The proposed research will explore the effects of several personal (including gene polymorphisms), occupational and psychosocial factors as well as their interactions on LBP in workers.

2.3 Methodology

2.3.1 Participants

Sixty participants were recruited for the study (Table 2.3). Participants were patients already suffering from LBP and some of them had a previous lumbar MRI taken. Both males and females over the age of 18 were eligible. Pregnant females were not allowed to participate due to the confounding effect of hormones on low back pain. Other eligibility criteria also required that participants were currently in or were in jobs involving manual labor, prolonged sitting/standing and suffering from low back pain. Participants were compensated $50 for completing the study protocols.

Table 2.3 Participant demographics

Demographic	Males (n=26)	Females (n=34)	Total (n=60)
Age (years)	50.30 (15.88)	44.62 (16.19)	47.08 (16.17)
Height (inches)	70.08 (3.26)	64.71 (2.43)	67.03 (3.87)
Body mass (lbs)	202.31 (35.59)	170.94 (33.85)	184.53 (37.73)
BMI	28.96 (4.71)	28.78 (5.86)	28.86 (5.35)

Note: Values are mean (SD)

2.3.2 Independent Variables

The independent variables involve personal, occupational and psychosocial factors information obtained from the participants.

2.3.2.1 Personal Factors

Age, gender, Body Mass Index (BMI), family history of low back pain, physical activity level, alcohol consumption and smoking habits were obtained using a custom demographic questionnaire (see Appendix C). BMI was calculated from the height and weight measurements taken using the following equation: BMI = weight (kgs) / height $(m)^2$ and the numeric value obtained served as the variable. Family history of LBP was denoted with a 'yes' or a 'no'. Physical activity level, smoking and alcohol consumption are ordinal variables that fell into one of the categories which were assigned a number according to the level of each. Actual levels were combined to obtain two levels for each variable to be used in data analysis due to homogeneity of the data (Table 2.4) (see Appendix K).

Table 2.4 Levels used to categorize physical activity, smoking and alcohol consumption in the questionnaire

Physical Activity Levels		**Smoking Levels**		**Alcohol Consumption Levels**	
Actual	*Combined*	*Actual*	*Combined*	*Actual*	*Combined*
< 3 times a week (short workouts)	No to Low	None	No	Abstain	No
< 3 times a week (long workouts)		< 5 a day	Yes	Light – 3/week	Yes
3 to 5 times a week (short workouts)		5 to 10 a day		Moderate – 4 to 14/week	
3 to 5 times a week (long workouts)	Moderate to High	10 to 15 a day		Heavy – >14/week	
> 5 times a week (short workouts)		> 15 a day			
> 5 times a week (long workouts)					

Genetic information was obtained from the DNA of each participant via blood draws. More details are provided under section 2.3.4 for procedures. Out of the four genes, responses for two genes (COL9A3 and IL1-RN), were either a yes or no indicating presence or absence of the polymorphism (i.e., 2 levels). The AGC1 gene consists of different repeat regions ranging from 13 to 33 and the response was a number from 13 to 33 as determined from the gene analysis. Due to homogeneity of the data, the repeat lengths were grouped into less than and greater than 25 (i.e., 2 levels). This was done based on the studies that identified that shorter alleles (25 repeats or less) were linked to severe cases of LBP (Eser et al., 2010; Kawaguchi et al., 2002; Mashayeki et al., 2010). The VDR gene had a 'Taq', 'Fok' or no polymorphism response (i.e., 3 levels).

2.3.2.2 Occupational Factors

Force, posture, repetition and vibration exposures at work were collected using a demographic questionnaire. The RULA worksheet was used as a general template to record force, posture and repetition exposures (McAtamney and Nigel Corlett, 1993).

Sections relating to the trunk were extracted from the the RULA worksheet and scoring metrics were retained (see Appendix J). Force was scored based on the weight of the load lifted, if it was static/intermittent and the average time; and ranged from 0 to 7. Possible posture scores ranged from 1 to 10 and took into account trunk angle, twisting/side bending, and the average time the posture was assumed. Repetition scores ranged from 1 to 7 and was obtained based on the cycle time and duration of exposure. Exposure to whole body vibration was determined as being present (yes/no response - scored 1 and 0) and the amount of time on the job that the participant was exposed (<2 hours/day, 2-4 hours/day, 4-8 hours/day and >8 hours/day – scored 1 through 4). A vibration score was determined by adding the yes/no response score and the score for the amount of time exposed, and vibration scores ranged from 0 to 5. A combined final score also served as a variable. Due to homogeneity of data, the factors were converted into categorical data. Force was divided into 'low' (scores 0 to 4) and 'high' (scores 5 to 7) categories, posture was converted to 'close to neutral' (scores 1 to 5) and 'non-neutral' (scores 6 to 10) categories, and repetition and vibration was converted into 'yes' or 'no' categories indicating presence or absence.

2.3.2.3 Psychosocial Factors

The Perceived Stress Scale (PSS) Questionnaire (Cohen et al., 1983) (see Appendix D) and the Job Content questionnaire (Karasek et al., 1998) (see Appendix E) were used to quantify exposure to psychosocial risk factors at work. The PSS consists of 14 questions that were scored according to the guidelines and a final score (ranging from 0 to 56) was used as the variable. Higher score represent higher exposures to psychosocial risk factors. The recommended 'Standard Job Content Instrument' version

of the JCQ was used, to which the job dissatisfaction section was added. The sections included were decision latitude, physical job demands, psychological job demands, social support, organizational level, job dissatisfaction, and job insecurity. Each section was scored separately according to the scoring guidelines those scores were used in later analyses.

2.3.3 Dependent Variables

The dependent variables for this study included both physician and self-reported severity ratings of LBP.

2.3.3.1 Physician Ratings of LBP

Injury presence was assessed using magnetic resonance imaging (MRI) for those participants who already had MRI scans of the low back taken. Physician based severity ratings of the disorder based on MRI scans were used in analyses. The MRI was rated by Dr. Butler. On obtaining authorization (see Appendix B – Informed Consent) from the participant for disclosure of MRI information, the researcher gained access to the interpretations. Severity scores ranged from 0 to 4 indicating no, mild, moderate and severe ratings. Presence or absence of canal stenosis and nerve impingement were also evaluated and used as variables in analysis.

2.3.3.2 Self-Reported Ratings of LBP

The Oswestry low back pain scale (see Appendix F) and VAS pain scales (Appendix G) served as the self-reported ratings of LBP severity. The ODI is a 10 item questionnaire with a 6-point ordinal scale ranging from 0 (no pain while doing activity) to 5 (pain prevents doing activity) that is used to assess back pain (Grotle et al., 2004) and

was completed by the participant. A total score of 50 is possible and the final score obtained was expressed as a percentage value by summing the value of each item, dividing by 50 and multiplying by 100.

Pain severity ratings were also obtained through a 10 cm visual analog scale (VAS) (see Appendix G) having anchors at 'No pain' and 'Worst imaginable'. The scale was scored manually by measuring the distance from the no pain anchor to the mark made by the participant denoting pain severity. The value obtained was recorded in mm.

2.3.4 Procedures

Participants were recruited via a local physician and through local announcements, and were provided with the researcher's contact information. Those individuals who contacted the researcher were read the informed consent over the phone and were asked eligibility criteria if they expressed a willingness to participate. Those who met the study requirements were asked to meet the researcher at the Longest Student Health Center on MSU's campus. Formal informed consent documents were completed which also contained a section where authorization for disclosure of protected health information (PHI) was obtained. This was required for the physician to release severity ratings based on the MRI readings to the researcher. The participants were then asked to complete a short questionnaire that included basic information (e.g., age, gender, race, height, weight, personal habits etc.). They were also asked to complete a pain questionnaire as well as perceived stress and job stress questionnaires and a pain severity VAS. A blood sample of 5ml was collected from them by a phlebotomist at the Health Center using clinical procedures. The blood was stored in tubes containing an anti-coagulant and stored in a freezer. The tubes were labeled in codes.

The blood samples were then shipped to BioServe (9000 Virginia Manor Road, Beltsville, MD) where DNA extraction was carried out. The DNA samples obtained were stored in a BSL-certified laboratory at the Institute for Genomics, Biocomputing and Biotechnology (IGBB) where further processing (explained under section 2.3.4.1), PCR and electrophoresis, was carried out. The samples were then sent for sequencing. Analysis of all other data collected was done in the Human Systems Engineering Laboratory (300 McCain).

2.3.4.1 Gene Data Protocols

Aggrecan Gene: The polymorphism in the aggrecan gene (AGC1) is a repeat region of about 57 base pairs in exon 12. This region was amplified to look for differences in the length of repeat regions using PCR analysis (Doege, Coulter, Meek, Maslen, & Wood, 1997). Primers to be used as well as the PCR amplification protocol were obtained from previous literature and are given below (Kawaguchi, et al., 1999):

- Sense primer: 5'-TAGAGGGCTCTGCCTCTGGAGTTG-3'
- Antisense primer: 5'-AGGTCCCCTACCGCAGAGGTAGAA-3'

PCR Amplification Protocol:

- Materials: The 50 µl PCR reaction mixture containing
    - 50 pmol of each of the sense and antisense primers,
    - 100 ng of genomic DNA,
    - 0.2 mM dNTPs,
    - 0.1% Triton X-100,
    - 2.5 units of a high fidelity *Taq* DNA polymerase,
    - 10 mM Tris-HCl, pH 8.3,

- 1.5 mM MgCl2, and
- 50 mM potassium chloride.

- Steps: 30 cycles
  - Denaturation at 95 C for 0.5 minutes
  - Annealing at 67 C for 0.5 minutes
  - Extension at 72 C for 1.5 minutes

The PCR products obtained were then analyzed using a 2% agarose gel and stained using ethidium bromide. The length of the repeat regions of the gene for each participant was the output.

Vitamin D Receptor Gene: The polymorphisms in the Vitamin D Receptor (VDR) gene are known as the Fok1 in exon 2 and the Taq1 in exon 9. Exon 2 which is about 266 base pairs and exon 9 which is about 484 base pairs were amplified to look for the Fok1 and Taq1 polymorphisms using a PCR assay. Primers, PCR amplification protocols and assays were obtained from previous literature and are given below (Eser, et al., 2010):

Fok1:

- Forward primer: 5'-AGCTGGCCCTGGCACTGACTCTGCTCT-3'
- Reverse primer: 5'-ATGGAAACACCTTGCTTCTTCTCCCTC-3'

Taq1:

- Forward primer: 5'-CAGAGCATGGACAGGGAGCAAG-3'
- Reverse primer: 5'-CGGCAGCGGATGTACGTCTGCAG-3'

PCR Amplification Protocol:

- Materials: The 50 µl PCR reaction mixture containing
  - 10 pmol of each of the sense and antisense primers,
  - 5 µl of genomic DNA,

- 25 mM dNTPs,
- 0.1% Triton X-100,
- 0.5 µl of a high fidelity *Taq* DNA polymerase,
- 25 mM $MgCl_2$, and
- 10X PCR buffer

- Steps: 30 cycles
  - Denaturation at 95 C for 0.5 minutes
  - Annealing at 62 C for 0.5 minutes
  - Extension at 72 C for 1.5 minutes

The PCR products obtained were digested with endonucleases (Taq1 and Fok1) and then analyzed using a 2% agarose gel and stained using ethidium bromide. Presence of the Taq, Fok or no polymorphism was the output.

Collagen Gene: The polymorphism in the collagen gene (COL9A3) is a mutation that is present in exon 5 that leads to an arginine (position 103) to tryptophan substitution (trp3 allele) containing a C→T sequence variation (CGG→TGG). The region amplified was about 209 to 411 base pairs. Primers and PCR amplification protocols were obtained from previous literature and are given below (Paassilta, et al., 1999):

- Forward primer: 5'- CACCAAGGGAAGGGTCCGTGC -3'
- Reverse primer: 5'- CTACCAGCTCCTTGGCCTTGTGG -3'

PCR Amplification Protocol:

- Materials: The 30 µl PCR reaction mixture containing
  - 60 ng genomic DNA,
  - 5 pmol each primer,
  - 200 µM dNTP,

- 1.5 mM MgCl, and
- 1 U a high fidelity *Taq* polymerase

- Steps: 35 cycles
  - Denaturation at 94.5 C for 40 seconds
  - Annealing at 60 C for 50 seconds
  - Extension at 72 C for 1 minutes
  - Final extension 72 C for 10 minutes

The PCR products obtained were directly sequenced to look for the substitution (Aladin, et al., 2007; Matsui, et al., 2004).

Interleukin1 Gene: The polymorphism in the interleukin gene (IL1-RN) is a mutation that is present in the exon containing the IL-1RNA^{1812} region and has a G^{1812}→A sequence variation. Primers and PCR amplification protocols were obtained from previous literature and are given below (Solovieva, et al., 2004):

- Forward primer: 5'-GCATCAAGTCAGCCATCAGC -3'
- Reverse primer: 5'-CCAGAGCCTGAAAGCATTTG -3'
- Detection primer: GGACTGTGGCCCAGGTACT

PCR Amplification Protocol:

- Materials: The 15 µl PCR reaction mixture containing
  - 3 pmol of each of the sense and antisense primers,
  - 40 ng of genomic DNA,
  - 3 nmol dNTPs,
  - 0.3 units of a high fidelity *Taq* DNA polymerase,
  - 1 X PCR buffer

- Steps: Touchdown program of 35 cycles

- Denaturation at 95 C for 30 seconds
- Annealing from 65 to 53 for 30 seconds
- Extension at 68 C for 2 minutes

The PCR products obtained were directly sequenced to look for the substitution (Aladin, et al., 2007; Matsui, et al., 2004).

2.3.5 Data Analysis

Appropriate descriptive statistics (e.g., mean, standard deviation, minimum, maximum, frequency counts, etc.) were determined for all variables. Prior to analysis, diagnostic and normality tests were conducted. Scatter plots, residual plots, normal quantile plots and histograms were generated, and all data were found to meet normality assumptions, excluding the JCQ section scores and VAS scores. Transformations were unsuccessful in achieving normality. The analyses used here (ANOVA and regression) are known to be robust to normality assumptions, these data were used in their raw format. All analysis was done using the Statistical Analysis Software (SAS) 9.2 and JMP 7 software from SAS. An alpha level of 0.1 was used to determine statistical significance. Details for each dependent variable analysis are provided below.

2.3.5.1 Subjective Severity Ratings: ODI and VAS

Linear regression analysis was first conducted on the two continuous variables, age and BMI, to determine if a significant relationship existed with both subjective severity measures. Age was found to be significant and BMI approaching significance for ODI measures. Therefore, a linear model ANOVA was performed to determine the

effects of all personal factors studied on ODI and VAS. Age was included as a continuous variable and BMI was converted into the generally accepted categories (ideal, overweight and obese) (WHO, 1995). All two-way interactions were also analyzed. Significant effects were further explored with a post-hoc analysis using Tukey's Honestly Significant Difference (HSD) test where appropriate.

The genes, although considered personal factors, were analyzed separately and in combination to further quantify their role in LBP severity. One-way ANOVA was performed on each of the 4 genes (AGC1, VDR, COL9A3 and IL1-RN) to investigate effects of each of the genes on the ODI and VAS measures. Factorial ANOVA was conducted to study the cumulative effects of the genes and interactions on the LBP severity measures. Two-way interactions were also analyzed where possible. Tukey's HSD post-hoc analysis was used to further explore any significant effects.

Two analyses were conducted for the occupational factors. First, linear regression analysis was performed to determine the effect of the final combined occupational score on ODI and VAS ratings. Secondly, a factorial ANOVA was performed on the four occupational risk factors: posture, force, repetition and vibration. All two-way interactions were also analyzed.

Linear regression analysis was also performed on each section score of the JCQ, and the PSS score. Prior to analysis correlations were determined between the psychosocial variables to address multicollinearity issues. Since PSS was found to be significantly correlated with all the factors from the JCQ, simple linear regression was conducted on each factor individually to look for significant relationships between the factors and severity.

2.3.5.2 Physician Ratings: MRI

Logistic regression was used to study the effects of each of the personal, genetic, occupational and psychosocial factor effects on the 2 dichotomous variables, stenosis and nerve impingement. Polytomous logistic regression was conducted on the polytomous variable MRI severity. Full models were run for personal, genetic and psychosocial factors considering only the main effects. For the occupational factors a full model considering all main effects and two-way interactions was run.

2.3.5.3 Correlations between Severity Measures

Spearman's correlation coefficient (r) was calculated to determine correlations between the subjective and objective measures of pain severity. The data for these measures are not expected to be linear and may not meet all the assumptions to use Pearson's correlation, therefore, Spearman's correlation was used. The subjective and objective measures data were correlated in order to determine whether injury severity as seen on the MRI readings correspond to the pain severity ratings that were obtained through self-report by the patients through the questionnaire and VAS.

2.4 Results

2.4.1 Subjective Severity Ratings: ODI and VAS

2.4.1.1 Personal Factors

Descriptive statistics showed an increase in pain severity levels with age for ODI. For the VAS measures, a decrease was observed with age. No differences in LBP severity between males and females was observed for both ODI and VAS. LBP severity was found to increase with an increase in BMI. However, the increase from the ideal to

the overweight category was more drastic than between the overweight and obese categories for the ODI measures. For the VAS measures, an increase was observed from the overweight to obese categories. Participants with a family history of LBP reported higher levels of ODI severity than those without but the opposite was observed for VAS. Increased levels of physical activity were observed to have no effect on the ODI severity ratings but an increase was seen for VAS ratings. Participants who consumed alcohol and who smoked had higher LBP severity ratings than those who abstained and did not smoke (Table 2.5).

Table 2.5 Descriptive statistics of personal factors. Values are Mean (SD)

Independent Variable	Level	N	ODI	VAS
Age	18 to 49 years	33	37.57 (16.09)	8.12 (1.49)
	50 to 65 years	20	45.50 (16.03)	7.51 (1.97)
	Above 65 years	7	48.00 (13.42)	7.81 (1.82)
Gender	M	26	41.54 (16.26)	7.82 (1.67)
	F	34	41.35 (16.30)	7.93 (1.74)
BMI	Ideal (Below 25)	13	36.92 (13.99)	7.81 (0.99)
	Overweight (25 to 30)	24	42.00 (18.89)	7.70 (1.98)
	Obese (Above 30)	23	43.39 (14.24)	8.11 (1.73)
Family History	Yes	36	43.22 (14.81)	7.74 (1.70)
	No	24	38.75 (17.94)	8.09 (1.71)
Physical Activity	No to Low	42	41.43 (15.72)	7.74 (1.76)
	Moderate to High	18	41.44 (17.57)	8.21 (1.54)
Smoking	No	42	37.86 (14.55)	8.13 (1.48)
	Yes	18	49.78 (16.98)	7.31 (2.06)
Alcohol	No	27	36.07 (12.95)	7.58 (1.65)
	Yes	33	45.82 (17.32)	8.12 (1.71)

Simple linear regression analysis of the variables age and BMI showed that age was significant (p-value 0.060) and BMI was approaching significance (p-value 0.15) for the ODI measures (Figure 2.2). For VAS, both age and BMI were not found to be significant.

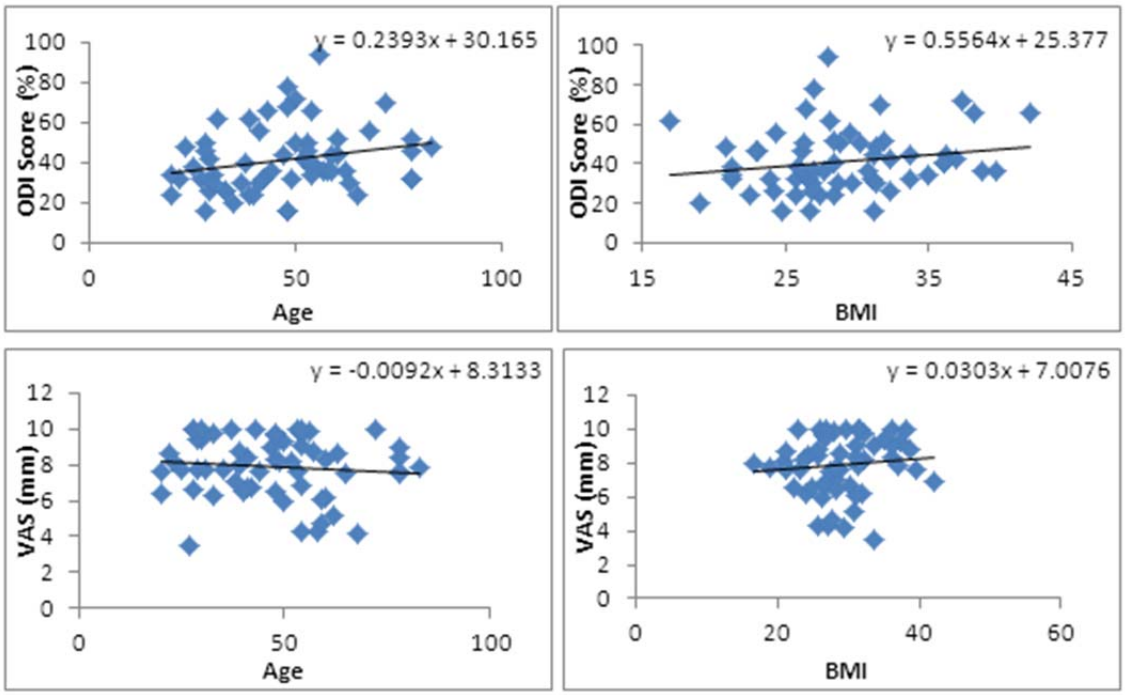

Figure 2.2 Scatter plots for Age vs. ODI/VAS and BMI vs. ODI/VAS

Results of the linear model ANOVA showed a significant model (p-value 0.06). Age was found to significantly affect ODI ratings. Several interaction effects were also found (Table 2.6). For the VAS ratings, the model was not found to be significant with a p-value 0.95 (Table 2.6).

Table 2.6 Linear Model ANOVA results. Values are p-values

Independent Variable	ODI	VAS
Age	**0.0196**	0.7359
Gender	0.4650	0.7204
BMI	0.7019	0.8513
History	0.1415	0.9015
Physical Activity	0.3528	0.7756
Alcohol	0.7598	0.7499
Smoking	0.3788	0.3690
Age*Gender	0.9181	0.9052
Age*BMI	0.4477	0.9486
Age*History	0.2642	0.8985
Age*Activity	0.4050	0.8749
Age*Alcohol	0.1530	0.9954
Age*Smoking	0.8766	0.5186
Gender*BMI	0.2675	0.9001
Gender*Alcohol	0.5887	0.3284
Gender*History	0.2971	0.6126
Gender*Activity	**0.0743**	0.7119
Gender*Smoking	**0.0383**	0.5928
BMI*History	**0.0103**	0.5550
BMI*Activity	**0.0056**	0.9998
BMI*Alcohol	0.8766	0.5827
BMI*Smoking	**0.0229**	0.8815
History*Activity	**0.0497**	0.2034
History*Alcohol	**0.0367**	0.9856
History*Smoking	**0.0695**	0.7893
Activity*Alcohol	0.1485	0.4399
Activity*Smoking	0.1796	0.3227
Alcohol*Smoking	**0.0477**	0.1779

Note: Bolded values indicate significant differences.

A significant interaction effect of gender and physical activity, and gender and smoking was found. However, Tukey's comparisons did not show any significant differences. Interaction effects of BMI with family history, BMI with physical activity and BMI with smoking were found to be significant. Participants in the obese category with no family history of LBP had significantly lower ratings from those in the overweight category and no family history. They also had significantly lower ratings

from those in the obese category but with a family history. Only those participants in the overweight and obese categories had significant differences between the low and high physical activity levels. Those in the overweight category and who were more active reported higher ratings than those in the obese category and who were more active. Higher ratings were also seen for those who were more active and in the overweight category when compared to those who were less active and in the overweight category. Participants who smoked and were in the overweight category had significantly higher ODI ratings than those who smoked and were in the obese category. Family history also significantly interacted with physical activity, alcohol and smoking to affect ODI ratings. Pairwise comparisons showed that severity ratings of those participants with no family history of LBP and who did not consume alcohol was significantly lower than those with no family history but who consumed alcohol. An interaction effect of smoking and alcohol was also significant and showed that participants who consumed alcohol and smoked had significantly higher ODI ratings that those who only smoked.

2.4.1.2 Gene Factors

2.4.1.2.1 Aggrecan (AGCI)

The repeat regions in the population studied ranged from 19 to 28, with 27 and 28 repeats most common. Frequencies are given in table. The data of 14 participants (23%) was lost due to failure of amplification of the DNA in PCR as confirmed in the agarose gel electrophoresis (see Appendix L). An increase in the number of repeats showed a general decreasing trend for VAS. In case of ODI, a decrease was seen from 21 to 27 repeats (Table 2.7). One-way ANOVA conducted on the aggrecan gene did not yield significant results. The p-values obtained for ODI was 0.7417 and for VAS was 0.3616.

Table 2.7 Descriptive statistics of gene factors. Values are mean (SD)

Gene	Level	N	ODI	VAS
AGC1	19	1	36.00 (-)	8.74 (-)
	21	5	47.60 (13.52)	8.37 (1.84)
	25	7	46.00 (13.22)	8.16 (1.54)
	27	12	41.67 (23.77)	7.77 (2.14)
	28	21	45.43 (13.55)	7.8 (1.44)
VDR	Taq	32	44.75 (18.91)	7.88 (1.83)
	No	22	40.00 (11.11)	7.86 (1.53)
COL9A3	Yes	3	42.67 (11.01)	8.12 (0.47)
	No	52	42.65 (16.50)	7.91 (1.73)
IL1-RN	No	52	41.02 (14.74)	7.84 (1.72)
	Yes	3	49.33 (38.80)	8.64 (1.18)

2.4.1.2.2 Vitamin D Receptor (VDR)

Only the presence or absence of the taq polymorphism is reported as the fok restriction digestion did not yield results as confirmed by the agarose gel electrophoresis (see Appendix L). For the taq polymorphism, the data of 5 participants (8.3%) was lost. An increasing trend for both ODI and VAS was observed with the presence of the taq polymorphism where the presence of the polymorphism showed higher severities (Table 2.7). One-way ANOVA conducted on the VDR gene did not yield significant results. A p-value for ODI of 0.2952 and a p-value for VAS of 0.9683 were obtained.

2.4.1.2.3 Collagen (COL9A3)

PCR amplification of the DNA was carried out and 55 were successfully amplified (8% of data was lost) (see Appendix L). Only 3 out of the 55 participants had the arginine (position 103) → tryptophan substitution (trp3 allele) containing a C→T sequence variation (CGG→TGG). Presence of the polymorphism in the gene showed a higher mean VAS value (Table 2.7). One-way ANOVA conducted on the COL9A3 gene

did not yield significant results. A p-value for ODI of 0.9554 and a p-value for VAS of 0.8369 were obtained.

2.4.1.2.4 Interleukin 1 (IL1-RN)

PCR amplification was successful for 55 of the samples (8% of data was lost) (see Appendix L). Out of the 55, only 3 showed the gene polymorphism $G^{1812} \rightarrow A$ at nucleotide position 1812. Presence of the polymorphism in the gene showed higher mean ODI and VAS values (Table 2.7). One-way ANOVA conducted on the Il-1RN gene resulted in non-significant p-values of 0.4028 for ODI and 0.4199 for VAS.

2.4.1.2.5 Cumulative Effects

Factorial ANOVA conducted on ODI resulted in a non-significant model with a p-value of 0.9249. For VAS, the same was obtained with a p-value of 0.4846. P-values are presented in table 2.8. Interaction effects were not tested due to the limitations of the small sample size.

Table 2.8 Factorial ANOVA results. Values are p-values

Independent Variable	ODI	VAS
AGC1	08443	0.1132
VDR	0.5321	0.8028
COL9A3	0.8462	0.7781
IL-1RN	0.6790	0.3899

2.4.1.3 Occupational Factors

Descriptive statistics for the four occupational risk factors showed that higher ODI severity levels were reported when higher force requirements, presence of repetition and vibration and use of non-neutral postures were required on the job (Table 2.9). In case of VAS, the opposite was observed (Table 2.9).

Table 2.9 Descriptive statistics of occupational factors. Values are Mean (SD)

Independent Variable	Level	N	ODI	VAS
Force	Low	33	35.82 (13.69)	7.88 (1.78)
	High	27	48.30 (16.49)	7.88 (1.62)
Posture	Close to neutral	26	34.61 (12.97)	8.15 (1.51)
	Not neutral	34	46.65 (16.55)	7.67 (1.82)
Repetition	Yes	26	44.15 (13.09)	7.40 (1.82)
	No	34	39.35 (18.05)	8.25 (1.52)
Vibration	Yes	13	43.54 (12.00)	7.77 (1.78)
	No	47	40.85 (17.18)	7.91 (1.69)

Linear regression analysis done on the final occupational score yielded a significant model (p-value of 0.0138 but with and R^2 of only 0.1 (Figure 2.3) for ODI. For VAS, a non-significant model with a p-value of 0.1693 and R^2 of 0.03 was obtained. Linear regression was also conducted on the scores for force and posture and were found to be significant for ODI (posture – p-value of 0.006 and force p-value of 0.02) but not significant for VAS (posture – p-value of 0.30 and force p-value of 0.54). Scores were combined to form 2 categories for each variable: low and high force requirements, and close to neutral and non neutral postures and were used in the ANOVA analysis.

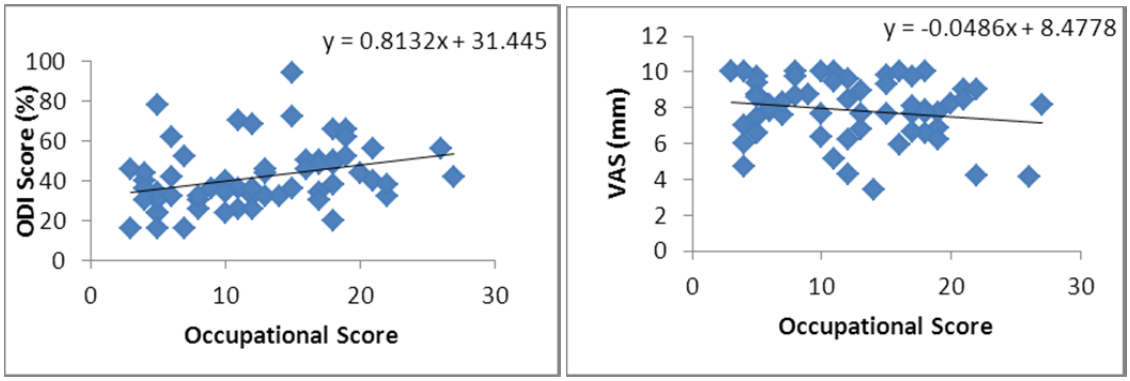

Figure 2.3 Scatter plots for occupational score vs. ODI

Factorial ANOVA conducted on force, posture, repetition and vibration resulted in significant model with a p-value 0.02 for ODI. For VAS, the p-value of model was 0.5341 and was not significant. Interaction effects of force and posture, and force and repetition were found to be significant (Table 2.10). Tukey's post hoc analysis showed that having both high force requirements and non-neutral postures on the job resulted in significantly higher severity ratings than having either a high force and close to neutral postures, or low force and non neutral postures on the job.

Table 2.10 Factorial ANOVA results. Values are p-values

Independent Variable	ODI	VAS
Force	0.6573	0.8263
Posture	0.2283	0.1985
Repetition	0.3433	0.1343
Vibration	0.3148	0.3912
Force*Posture	**0.0367**	0.2808
Force*Repetition	**0.0779**	0.8878
Force*Vibration	0.8843	0.2473
Posture*Repetition	0.9801	0.3906
Posture*Vibration	0.1603	0.5736
Repetition*Vibration	0.7778	0.7720

2.4.1.4 Psychosocial Factors

Descriptive statistics showed an increasing trend in ODI ratings for PSS, physical and psychological demands, job dissatisfaction and job insecurity. A decreasing trend was seen with an increase in decision latitude, social support and organizational level. In general, the opposite was observed for the VAS ratings (Table 2.11).

Spearman's correlations were calculated between all the variables and it was found that the PSS score was significantly correlated with all the other variables (Table 2.12). Therefore, simple linear regression of each variable vs. ODI was conducted in order to avoid multicollinearity issues. Results showed that only PSS (p-value = 0.0006), job dissatisfaction (p-value = 0.08) and job insecurity (p-value = 0.06) were significant for ODI ratings (Table 2.13, Figure 2.4). Results of simple linear regression showed that none of the variables significantly affected the VAS ratings (Table 2.13).

Table 2.11 Descriptive statistics of psychosocial factors. Values are Mean (SD)

Independent Variable	Categories	N	ODI	VAS
Perceived Stress	0 to 19	11	31.45 (16.76)	8.59 (1.17)
	20 to 29	25	38.32 (12.56)	7.64 (2.01)
	30 to 50	24	49.25 (16.12)	7.81 (1.50)
Decision Latitude	40 to 60	11	45.45 (14.62)	7.57 (1.62)
	61 to 80	39	41.08 (17.17)	7.81 (1.83)
	81 to 100	10	38.40 (14.01)	8.50 (1.10)
Physical Demands	5 to 10	18	36.67 (18.60)	8.19 (1.58)
	11 to 15	26	41.92 (11.61)	7.50 (1.99)
	16 to 20	16	46.00 (18.93)	8.15 (1.19)
Psychosocial Demands	0 to 7	17	40.70 (20.30)	7.77 (1.53)
	8 to 14	38	41.05 (14.77)	7.99(1.81)
	15 to 21	5	46.80 (11.80)	7.40 (1.54)
Social Support	0 to 20	9	44.67 (9.33)	7.52 (1.62)
	21 to 30	21	39.81 (14.28)	7.94 (1.81)
	Above 30	30	41.60 (18.98)	7.94 (1.68)
Organizational Level	20 to 30	22	46.27 (17.27)	8.05 (1.66)
	31 to 50	27	36.81 (12.57)	7.77(1.73)
	51 to 70	11	43.09 (19.70)	7.80 (1.80)
Job Dissatisfaction	0 to 0.2	31	36.84 (14.82)	7.83 (1.64)
	0.2 to 0.6	23	44.87 (16.12)	7.76 (1.86)
	0.6 to 1	5	48.00 (15.74)	8.46 (1.50)
Job Insecurity	-1 to 2	45	39.55 (16.50)	7.97 (1.70)
	3 to 5	9	49.78 (8.92)	8.03 (1.24)
	6 to 12	6	43.00 (14.01)	6.99 (2.21)

Table 2.12 Spearman's correlation coefficients for Psychosocial factors

	PSS	DL	DPh	Dps	SS	OL	JD	JI	ODI	VAS
PSS	1.00	**-0.32**	**0.47**	**0.29**	**-0.29**	**-0.21**	**0.55**	**0.43**	**0.47**	-0.03
DL		1.00	-0.18	0.02	**0.25**	**0.37**	**-0.41**	-0.21	-0.13	0.19
DPh			1.00	0.15	-0.10	-0.17	**0.46**	0.15	**0.26**	-0.14
Dps				1.00	**-0.27**	-0.04	**0.39**	0.16	0.12	0.01
SS					1.00	**0.35**	**-0.47**	**-0.32**	**-0.28**	0.10
OL						1.00	**-0.41**	**-0.41**	**-0.26**	0.02
JD							1.00	**0.39**	**0.28**	0.12
JI								1.00	**0.33**	-0.09
ODI									1.00	0.08
VAS										1.00

Note: Bolded values indicate significant differences

Table 2.13 Simple linear regression results

Independent Variable	ODI			VAS		
	Slope	R^2	P-value	Slope	R^2	P-value
Perceived Stress	0.10	0.19	**0.0006**	-0.01	0.00	0.7376
Decision Latitude	-0.15	0.01	0.4533	0.03	0.04	0.1481
Physical Demands	0.79	0.04	0.1017	-0.05	0.02	0.3273
Psychological Demands	0.20	0.00	0.6823	-0.00	0.00	0.9179
Social Support	-0.20	0.04	0.1313	0.02	0.03	0.1956
Organizational Level	-0.13	0.01	0.4573	0.01	0.00	0.5977
Job Dissatisfaction	13.98	0.05	**0.0807**	0.49	0.00	0.5767
Job Insecurity	1.48	0.06	**0.0632**	-0.06	0.01	0.4530

Note: Bolded values indicate significant differences.

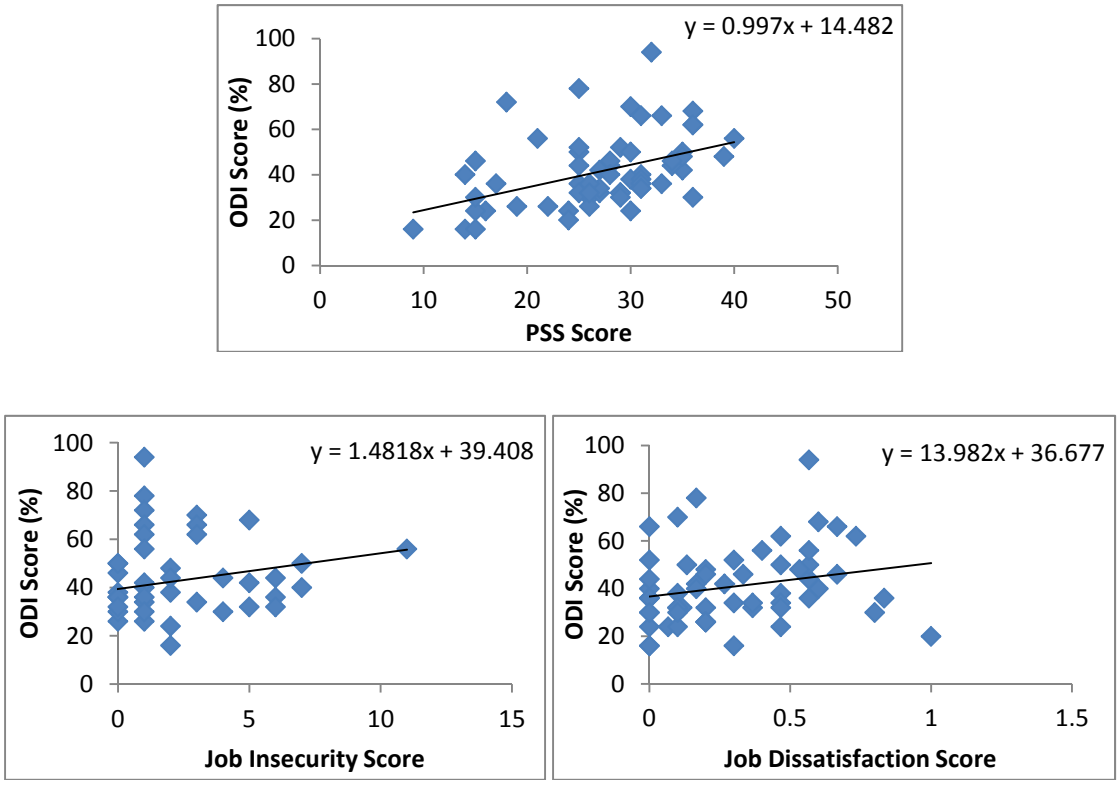

Figure 2.4 Scatter plots for PSS, job insecurity and job dissatisfaction vs. ODI

2.4.2 Physician Ratings: MRI Severity, Stenosis and Impingement

Only 36 out of the 60 participants had MRI records that were accessible and for which physician based severity ratings could be obtained.

2.4.2.1 Personal Factors

Descriptive statistics indicating the number of participants in each category for MRI severity, stenosis and nerve impingement broken down by factor is shown (Table 2.14). In general, it is observed that most participants (n = 28, 78%) fell into the mild severity level. Fewer participants were diagnosed with stenosis (n = 11, 31%) or nerve impingement (n = 9, 25%). All (100%) the participants in the above 65 years category had severe LBP. However, cases of stenosis and impingement were lower in this age group than the 50 to 65 group. All males (100%) were rated as having severe LBP, and had an increased number of stenosis and impingement cases than females. More cases of severe LBP and stenosis were common for those with a family history of LBP than those without. Fewer cases of severe LBP, stenosis and impingement were seen in those with higher physical activity levels. More cases of stenosis and impingement were observed in those who consumed alcohol.

Results of the logistic regression for the personal factors main effects showed that only physical activity significantly affected MRI severity ratings. Stenosis and nerve impingement were not found to be significantly affected by any of the variables (Table 2.15).

Table 2.14 Descriptive statistics of personal factors for MRI ratings

Independent Variable	Level	N	MRI Severity				Stenosis		Impingement	
			0	1	2	3	0	1	0	1
Age	18 to 49 years	22	2	19	1	0	18	4	16	6
	50 to 65 years	11	1	6	3	1	5	6	8	3
	Above 65 years	3	0	3	0	0	2	1	3	0
Gender	M	16	0	14	1	1	10	6	11	5
	F	20	3	14	3	0	15	5	16	4
BMI	Ideal (Below 25)	9	0	8	1	0	7	2	7	2
	Overweight (25 to 30)	14	2	11	0	1	9	5	11	3
	Obese (Above 30)	13	1	9	3	0	9	4	9	4
Family History	Yes	25	1	21	3	0	17	8	21	4
	No	11	2	7	1	1	8	3	6	5
Physical Activity	No to Low	24	1	22	1	0	16	8	17	7
	Moderate to High	12	2	6	3	1	9	3	10	2
Smoking	No	25	2	19	3	1	16	9	17	8
	Yes	11	1	9	1	0	9	2	10	1
Alcohol	No	17	2	12	2	1	12	5	14	3
	Yes	19	1	16	2	0	13	6	13	6

Table 2.15 Logistic regression results for personal factors. Values are p-values

Independent Variable	MRI Severity	Stenosis	Nerve Impingement
Age	0.2074	0.6257	0.3637
Gender	0.2225	0.4155	0.9691
BMI	0.1202	0.2221	0.4299
History	0.4259	0.4741	0.1578
Physical Activity	**0.0872**	0.3805	0.3307
Alcohol	0.6736	0.9792	0.8159
Smoking	0.9301	0.4219	0.3968

2.4.2.2 Gene Factors

2.4.2.2.1 Aggrecan (AGCI)

Out of the 46 participants with the AGC1 gene data, only 29 participants had MRI ratings. Descriptive statistics showed that 21 participants (72%) were in the mild severity category. Eight participants (31%) were diagnosed with stenosis and 7 (24%) with nerve impingement. Participants with shorter alleles (>25) were rarer (n= 7, 24%) (Table 2.16).

Those with shorter alleles were diagnosed with fewer cases of severe LBP but more cases of stenosis and impingement. Polytomous logistic regression conducted on MRI severity resulted in a non-significant model (p-value = 0.6694). Logistic regression models for stenosis and impingement were also non-significant (p-value = 0.2119 and 0.2887 respectively).

Table 2.16 Descriptive statistics of gene factors for MRI ratings

Independent Variable	Level	N	MRI Severity				Stenosis		Impingement	
			0	1	2	3	0	1	0	1
AGC1	21	4	1	2	1	0	2	2	2	2
	25	3	0	3	0	0	2	1	3	0
	27	9	1	5	3	0	6	3	6	3
	28	13	1	11	1	0	11	2	11	2
VDR	Taq	20	2	13	4	1	15	5	16	4
	No	13	1	12	0	0	9	4	9	4
COL9A3	Yes	1	0	1	0	0	1	0	0	1
	No	32	3	24	4	1	23	9	26	6
IL1-RN	No	33	2	27	4	0	23	10	24	9
	Yes	2	0	1	0	1	1	1	2	0

2.4.2.2.2 Vitamin D Receptor (VDR)

Out of the 54 participants with the VDR gene data, only 33 participants had MRI ratings. Descriptive statistics showed that 25 participants (76%) were in the mild severity category. Nine participants (27%) were diagnosed with stenosis and 8 (24%) with nerve impingement. Those with the presence of the taq polymorphism showed a slightly lower number of cases than those without the polymorphism. However, the higher severity levels were observed only in those with the taq polymorphism (Table 2.16). Regression

results did not in a significant model for any of the MRI measures (p-value = 0.2000, 0.7165, and 0.4832 for MRI severity, stenosis, and impingement respectively).

2.4.2.2.3 Collagen (COL9A3)

Out of the 55 participants with the COL9A3 gene data, only 33 participants had MRI ratings. Descriptive statistics showed that 25 participants (76%) were in the mild severity category. 9 participants (27%) were diagnosed with stenosis and 7 (21%) with nerve impingement (Table 2.16). The one participant with the polymorphism was diagnosed with both severe LBP and impingement. Logistic regression conducted on the MRI measures resulted in no significant regression models (p-values = 0.8367, 0.9814, and 0.9815 for MRI severity, stenosis, and impingement respectively).

2.4.2.2.4 Interleukin 1 (IL1-RN)

Out of the 55 participants with the IL1-RN gene data, only 35 participants had MRI ratings. Descriptive statistics showed that 28 participants (80%) were in the mild severity category. Eleven participants (31%) were diagnosed with stenosis and 9 (26%) with nerve impingement. Both of the participants with the polymorphism showed cases of severe LBP and 1 with a case of stenosis. The severity level of 3 was observed in the one with the polymorphism (Table 2.16). Logistic regression conducted on MRI severity resulted in a significant p-value of 0.0457, though stenosis and impingement models were not significant (p-values = of 0.5695 and 0.9754 respectively).

2.4.2.2.5 Cumulative Effects

Results of logistic regression on MRI severity showed that none of the gene factors were significant predictors of MRI severity. Logistic regression conducted on stenosis and impingement did not yield significant results. P-values are presented in table 2.17. Interaction effects were not tested due to the limitations of the small sample size.

Table 2.17 Logistic regression results for gene factors. Values are p-values

Independent Variable	MRI Severity	Stenosis	Impingement
AGC1	0.6356	0.3130	0.7537
VDR	0.4976	0.8828	0.5756
COL9A3	0.9524	0.9823	0.9742
IL-1RN	0.1277	0.4050	0.9650

2.4.2.3 Occupational Factors

In general, it was observed that hose involved in jobs with higher forces, non-neutral posture and the presence of repetition and vibration were diagnosed with cases of severe LBP (Table 2.18). More stenosis cases were associated with individuals that were exposed to lower forces, non-neutral postures, no repetition and the presence of vibration. More participants were found to have impingement when exposed to lower forces, neutral postures, and the presence of repetition and vibration.

The main effects of force, posture and repetition, as well as the interaction effects of force by posture and force by repetition significantly affected MRI severity ratings. Stenosis was significantly affected by only the force by posture interaction whereas nerve

impingement was not found to be significantly affected by any of the variables (Table 2.19).

Table 2.18 Descriptive statistics of occupational factors for MRI ratings

Independent Variable	Level	N	MRI Severity				Stenosis		Impingement	
			0	1	2	3	0	1	0	1
Force	Low	19	2	15	1	1	12	7	14	5
	High	17	1	13	3	0	13	4	13	4
Posture	Close to neutral	17	2	13	1	1	13	4	12	5
	Not neutral	19	1	15	3	0	12	7	15	4
Repetition	Yes	15	1	11	3	0	11	4	11	4
	No	21	2	17	1	1	14	7	16	5
Vibration	Yes	6	0	6	0	0	4	2	3	3
	No	30	3	22	4	1	21	9	24	6

Table 2.19 Logistic regression results for occupational factors. Values are p-values

Independent Variable	MRI Severity	Stenosis	Nerve Impingement
Force	**0.0229**	0.9673	0.8853
Posture	**0.0047**	0.7377	0.8384
Repetition	**0.0600**	0.4798	0.8372
Vibration	0.8942	0.8680	0.8748
Force*Posture	**0.0038**	**0.0601**	0.6046
Force*Repetition	**0.0484**	0.1996	0.4890
Force*Vibration	0.7132	0.8414	0.8674
Posture*Repetition	0.5400	0.1796	0.3089
Posture*Vibration	0.6207	0.9910	0.8582
Repetition*Vibration	0.6750	0.9791	0.8708

Note: Bolded values indicate significant differences.

2.4.2.4 Psychosocial Factors

In general, more cases of severe LBP, stenosis and impingement were observed in those participants reporting higher levels of exposure to psychosocial risk factors (Table 2.20). In case of PSS, it was observed that only 17% of stenosis cases were observed in the lowest level. Similarly, fewer cases were observed in the lower levels for decision latitude and social support. In fact, no cases of stenosis and impingement were seen in the lowest level of social support. Opposite trends were seen in job insecurity and job dissatisfaction where more cases were seen in the lower levels.

Table 2.20 Descriptive statistics of psychosocial factors for MRI ratings

Independent Variable	Level	N	MRI Severity				Stenosis		Impingement	
			0	1	2	3	0	1	0	1
Perceived Stress	0 to 19	6	1	3	1	1	5	1	4	2
	20 to 29	16	1	13	2	0	10	6	12	4
	30 to 50	14	1	12	1	0	10	4	11	3
Decision Latitude	40 to 60	5	1	4	0	0	4	1	4	1
	61 to 80	26	2	19	4	1	18	8	19	7
	81 to 100	5	0	5	0	0	3	2	4	1
Physical Demands	5 to 10	12	2	8	1	1	8	4	9	3
	11 to 15	11	0	9	2	0	9	2	11	0
	16 to 20	13	1	11	1	0	8	5	7	6
Psychosocial Demands	0 to 7	12	0	10	2	0	8	4	8	4
	8 to 14	22	3	17	1	1	16	6	18	4
	15 to 21	2	0	1	1	0	1	1	1	1
Social Support	0 to 20	5	2	3	0	0	5	0	5	0
	21 to 30	12	1	9	1	1	7	5	9	3
	Above 30	19	0	16	3	0	13	6	13	6
Organizational Level	20 to 30	13	2	9	2	0	7	6	8	5
	31 to 50	16	0	15	1	0	12	4	13	3
	51 to 70	7	1	4	1	1	6	1	6	1
Job Dissatisfaction	0 to 0.2	19	0	16	2	1	13	6	14	5
	0.2 to 0.6	16	3	11	2	0	11	5	13	3
	0.6 to 1	1	0	1	0	0	1	0	0	1
Job Insecurity	-1 to 2	26	3	20	2	1	19	7	20	6
	3 to 5	6	0	5	1	0	4	2	5	1
	6 to 12	4	0	3	1	0	2	2	2	2

Only MRI severity was significantly affected by psychosocial factors where PSS, physical demands, psychological demands and job dissatisfaction significantly affected MRI severity ratings. Stenosis and nerve impingement were not found to be significantly affected by any of the variables (Table 2.21).

Table 2.21 Logistic regression results for psychosocial factors. Values are p-values

Independent Variable	MRI Severity	Stenosis	Nerve Impingement
PSS	**0.0291**	0.6225	0.7580
Decision Latitude	0.1890	0.7989	0.7570
Physical Demands	**0.0590**	0.4553	0.4923
Psychological Demands	**0.0671**	0.6530	0.5860
Social Support	0.7372	0.1777	0.7751
Organizational Level	0.1667	0.1388	0.2630
Job Dissatisfaction	**0.0255**	0.6961	0.5631
Job Insecurity	0.1804	0.7594	0.6570

Note: Bolded values indicate significant differences.

2.4.3 Correlations between Severity Measures

The MRI ratings were not found to be significantly correlated with the subjective ratings of severity (Table 2.22). A moderate, inverse correlation was found between MRI severity ratings and VAS ratings (Table 2.22). A moderate correlation between MRI severity ratings and stenosis was also obtained (Table 2.22).

Table 2.22 Spearman's correlation coefficients for dependent variables

	ODI	VAS	MRI Severity	Stenosis	Impingement
ODI	1.00	0.14	-0.02	-0.23	0.00
VAS		1.00	**-0.36**	-0.06	0.22
MRI Severity			1.00	**0.31**	0.06
Stenosis				1.00	0.17
Impingement					1.00

2.5 Discussion

Personal and psychosocial factors, in addition to occupational factors, may influence LBP severity ratings, as seen in this study. A significant increase in ODI ratings was seen with age. Increased LBP severity with age is expected as the intervertebral discs undergo degenerative changes with aging (Grotle et al., 2004). The percentage of subjects with degenerated disks increased with age in a study and the increase was more rapid in subjects with LBP (Paajanen et al. 1997). Previous studies have also seen decreases in LBP severity ratings in the older population which corresponds with the observed VAS ratings obtained in this study where a slight decrease in VAS ratings was observed. VAS ratings represent the maximum pain felt by the participant whereas the ODI represents severity based on different activities. Possible explanations for decreased VAS ratings could be cognitive impairment, decreased pain perception and increased tolerance to pain (Leboeuf-Yde et al., 2009).

Higher ODI levels were observed in those participants with a family history of LBP but were not found to be significant. However, several significant interaction effects of family history were included in the model for ODI indicating that some hereditary component is involved in determining severity. On the other hand, although not

significant, it was observed that VAS severity ratings decreased in those with a family history of LBP, although, it cannot be said for sure why this was observed. A possible explanation would be that these participants tend to rate their worst pain less when compared to those without a history, since they have a better tolerance to the pain as they expect to be sufferers of LBP.

Obesity is a possible risk factor leading to LBP severity due to several reasons, such as higher mechanical stresses and abnormal loads on the spine due to the additional weight, loss of endurance, and reduced healing due to inability of blood flow and vital nutrients to reach injured areas because of the presence of fatty tissue (Orvieto et al., 1994; Manchikanti, 2000). An observed increase in subjective LBP severity was seen with BMI, although not significant. However, interaction effects of BMI on ODI were found and for the ODI differences were seen only among the overweight and obese categories.

Although no gender differences were observed from the descriptive statistics and it was not found to be significant, interaction effects of gender was seen on ODI severity. This may be explained by the fact that gender may influence the severity of LBP in the presence of other factors and not by itself. No gender differences in the subjective measures concur with general findings of previous research but are in contrast with other findings (Leboeuf-Yde et al., 2009; Wreje et al., 1997). These findings may have seen a larger number of women reporting LBP but not differences in severity levels which could explain why differences were not obtained. However, more females were present in this study compared to the males.

Though no main effects of physical activity were found on the subjective ratings, physical activity significantly affected MRI severity rating. Further, interaction effects of physical activity with family history of LBP, gender and BMI on ODI ratings were found which implies that physical activity, although not by itself but through interactions, may influence LBP severity. In particular, participants who were more active physically and in the overweight category had higher severity ratings than those who were less active and in the overweight categories. This shows that high physical activity may be associated with higher LBP severity at least in some populations which is in accordance with several studies that have reported a higher incidence of LBP and disc herniation in populations that exercised regularly. However, others have reported the opposite results (Manchikanti, 2000). The association of physical activity to LBP is not well understood and further investigations may be warranted.

Smoking and alcohol consumption as well as interaction effects of these were found to affect ODI ratings. Several mechanisms by which smoking affects LBP are suggested. A study noted breathing ability differences while handing loads may contribute to LBP as the muscles used for breathing are also used to maintain the spine. Therefore, smokers and others whose lung elasticity has been weakened may be at risk of LBP (McGill et al., 1995). A study saw that individuals with severe LBP were more likely to be smokers than non-smokers (Frymoyer et al., 1983) which was also observed in this study. Alcohol consumption may contribute to LBP by inducing uncoordinated movements altering biomechanical loads on the spinal structures. Further, alcohol consumption has been associated with psychosocial problems which are thought to contribute to LBP and chronicity. Interaction effects showed higher ODI ratings in those

who consumed alcohol than those who did not, and who had no family history of LBP indicating that alcohol consumption can influence reports of LBP severity. It was also found that participants who did both, consumed alcohol and smoked, had significantly higher ODI severity ratings that those who did either one.

The aggrecan, vitamin D receptor and collagen genes were not found to significantly affect LBP severity in this study. For the AGC1 gene, this is similar to previous studies (Videman, 1998) but in contrast to several other studies that found that the shorter repeats were over represented in the patients and also that shorter alleles were associated with higher severity levels, multilevel and severe disc degeneration (Eser etal., 2010; Kawaguchi et al., 2002; Mashayeki et al., 2010). Although a trend was seen where the shorter alleles showed higher severity levels, these were not significant. One reason why no differences were found could be that the previous studies looked at differences between control and patients as opposed to this study where the participants were patients with LBP of different levels. A reason for how shorter alleles could be linked to LBP is that since aggrecan is a major structural component of the intervertebral disc that provides the ability to resist compressive loads and osmotic pressure, a polymorphism resulting in shorter alleles may lead to the production of fewer number of the chondroitin sulfate chains that predisposes the disc to degeneration (Eser et al., 2010).

In case of the VDR gene, although not significant, the presence of the Taq1 polymorphism showed higher severity levels. A previous study has found that the presence of Taq1 polymorphism was more frequently associated with severe degeneration (Kawaguchi, et al., 2002). Another study saw that the presence of Taq1 polymorphism was linked to more degeneration based on MRI disc signal intensities

(Videman, 1998). It was seen that those without the polymorphism had a high bone-mineral density as opposed to those with the polymorphism who were at an increased risk of osteoporosis, which could be the reason for higher severity of LBP in those with the polymorphism. Further, it has been reported that the vitamin-D receptor is expressed both in osteoblasts and chondrocytes and that it may be directly involved in the differentiation, proliferation, and maturation of cartilage cells. Also, the intervertebral disc is rich in proteoglycans and vitamin D can influence proteoglycan synthesis, meaning that that the vitamin-D receptor may be directly involved in the pathophysiology of the degenerated intervertebral disc.

The SNP that was identified to be linked with LBP in the collagen gene was found to be present in only 3 participants and did not significantly affect any of the severity ratings. Insufficient data could be the reason for these results which is in contrast with previous findings (Paassilta, et al., 2001; Kales, et al., 2004; Solovieva, et al., 2006). Further, previous studies were conducted between cases and non-cases and compared the frequency of the presence of the SNP in both groups. Collagen is an important structural component of the intervertebral discs and therefore is considered an important gene to be studied to be linked to LBP. One reason why this partiular SNP is associated with LBP is because the mutation leads to an amino acid substitution (arginine to tryptophan) and tryptophan is a hydrophobic amino acid and is not generally found in collagen (Paassilta, et al., 2001).

The presence of the SNP in the interleukin gene showed higher levels of ODI and VAS ratings but was not significant. The only significant finding was of the IL-1 gene on MRI severity. Only 3 participants were found to have the SNP identified to be linked to

LBP. This is in accordance with previous studies which showed that those who were carriers of the SNP were at a higher risk of LBP and were associated with the occurrence of pain and the number of days with pain. It was also found to be associated with limitations to daily activities which is not supported by the results here as ODI was not found be significantly affected (Solovieva, et al., 2004). Herniated discs produce pain-inducing substances or inflammatory enzymes and IL-1RN may be required to inhibit the effects and control the inflammatory response. This may be how this gene may be linked to MRI-related LBP severity as seen in this study. The mutation may cause an underproduction which may lead to disc degeneration and pain.

Several reasons may exist for why no differences were found, one being the type of populations studied. Another reason may be the environment the population is present in and the inherent characteristics of the participants or other personal factors. Recent studies have shown that vibration has an additive effect with genetic risk factors (Virtanen, et al., 2007). Another study saw that lifestyle and genetic factors were associated with degeneration and LBP (Jones, 1998). These studies imply that not a single gene but gene-gene interactions and gene-environment interactions may be responsible. For this reason, it is believed that studying gene polymorphisms in relation to other risk factors such as personal, occupational and psychosocial may help understand LBP severity better.

However, when comparing the frequencies of the polymorphisms with existing studies, the numbers obtained in this study closely matched those of the previous findings. The percentage of participants in the current study with the AGC1 short alleles (<25) was 28% whereas those with the longer alleles was 72%. In a study conducted on a

Finnish population, the percentage of those with short and long alleles was 20 and 80% respectively (Solovieva et al., 2007). Another study in an Iranian population, had percentages of 24 and 76% (Eser et al., 2010). For the VDR gene, the percentage with the taq polymorphism was 59% and without was 41%. These exact numbers were obtained in a study involving both controls and patients in a Finnish population where 59% of the patients had the taq polymorphism (Noponen-Hietala et al., 2003). Kawaguchi et al., 2002 showed percentages of 63 and 35% for those with and without the polymorphism respectively in a patient population with reported herniation (Kawaguchi et al., 2002). Another study where spinal radiographs were used to identify cases of LBP, 61% of the patients had the polymorphism whereas 39% did not (Jones et al., 1998). The trp3 allele in the COL9A3 gene was present in only 5% of the population in this study. This allele was present in 14% of the population in the Noponen-Hietala study (Noponen-Hietala et al., 2003) and 12.3% in a study involving 86 patients and 65 controls (Paassilta et al., 2001). Two studies reported frequencies close to the one obtained here. One was where 4.3% of the patients had the trp3 allele (Kales et al., 2004) and the other reported that 6.5% had the allele out of all patients that participated (Matsui et al, 2004). Only 1 study was available with the IL-1RN gene data and reported a frequency of 44% with the SNP (Solovieva et al., 2004) which is much higher than the 5% obtained in this study.

It was observed that higher force, non neutral postures, and presence of repetition and vibration on the job resulted in higher ODI severity ratings but were not significant. However, force posture and repetition significantly affected MRI severity levels, and the interaction of force by posture significantly affected ODI and MRI severity levels as well as stenosis. Having both high force requirements and non neutral postures on the job lead

to higher severity ODI reports than from having either one individually. This is accordance with previous findings where lifting (force requirements) in addition to bending and twisting (posture), and when done repetitively was found to be more harmful. It was observed that the incidence of LBP in workers who performed heavy manual lifting was 8 times greater than workers with sedentary jobs (Manchikanti, 2000). An explanation for how bending can be harmful is that while bending, muscles are no longer active and only the soft tissues play a role. These types of tasks generate loads on the spine that exceed failure loads. In the aged workers, this further enhances their risk of injury (Pope et al., 2002).

Though trends were seen for the psychosocial factors and the subjective severity levels, only perceived stress, job dissatisfaction and job insecurity was found to significantly affect ODI ratings individually where increased levels resulted in increased severity reports. As expected, an increase in others factors such as social support, organizational level and decision latitude resulted in decreased ODI ratings but were not significant but still indicating that several psychosocial factors may influence LBP reporting. Perceived stress, job dissatisfaction, physical and psychological demands were also found to affect MRI severity ratings. Opposite but non- significant trends were seen for VAS ratings for which no solid reasons exist. Several possible mechanisms by which psychosocial factors can lead to LBP have been explained. Presence of psychosocial factors may influence changes in posture, movement and forces exerted which may impact biomechanical load. These factors can also elicit certain physiologic mechanisms, such as increased muscle tension or hormonal excretion that may influence pain perception. Presence of these factors may also affect the ability of an individual to cope

with pain and also influence reporting of symptoms (Hoogendoorn et al., 2000; Linton, 2001).

The study hypotheses were that the personal, genetic, psychosocial and occupational factors as well as their interactions within these categories would significantly affect the subjective and objective severity ratings. This was found to be true mainly only for the ODI ratings. In fact, the model was dominated by interaction terms and few individual risk factors were found to be significant for ODI.

The severity ratings, both subjective and objective, were not found to be significantly correlated. The VAS ratings represent the worst pain felt by the participant in their low back whereas the ODI represents severity based on different activities and therefore, ODI and VAS are measuring different things. Therefore a correlation may not have been obtained. Positive correlations between the physician based MRI ratings and subjective ratings was also expected but not found. Research has shown that some people who had spine abnormalities as seen in the MRI, experienced no symptoms of LBP (Jensen et al, 1994). This could be a reason why an inverse correlation, where an increase in MRI severity corresponded with a decrease in VAS rating, was seen. The LBP reported by workers is different from spine severities and is based on several factors that is not directly related to the physical abnormality of the spine and could be a reason why ODI was not correlated with the MRI ratings.

Previous models developed for other MSDs such as Carpal Tunnel Syndrome (CTS) found that interactions among different factors contributed to the disorder. It was also found that a mixed model including interaction terms was more accurate and had better predictive ability than the models with only personal or occupational risk factors

(Babski-Reeves and Crumpton-Young, 2003a, 2003b). Therefore, the next step would be to develop a predictive model for LBP including the interaction terms that were found to be significant. Although models incorporating different risk factors were developed previously, most models developed were logistic regression models to predict whether a person will or will not be a sufferer of LBP, but do not predict the severity level of LBP. In the present situation where a large percentage of the population report LBP, prediction of severity levels may be beneficial.

2.6 Limitations

The sample size is probably the biggest limitation of the study. The results may not have the accuracy that is required to generalize the results due to the limited sample size. However, the information obtained from this study will be beneficial for future studies.

The results that were expected for the genetic factors were not obtained and may be due to the fact that all participants were patients with LBP. A larger study involving both patients and controls may help in getting better findings. To our knowledge this is the first genetic study that investigated associations between previously identified genes (Aggrecan, VDR, Collagen and Interleukin) polymorphisms and LBP severity. However, larger studies are needed to confirm and validate findings.

The occupational factors were obtained through a questionnaire reported by the participants and not through any objective methods of data collection since the population being studied was a patient population with LBP and it would not be possible to subject them to tasks to study the effect of the occupational factors on them. Therefore, the data obtained was purely subjective. Psychosocial risk factors were obtained from 2

questionnaires: PSS and JCQ and the PSS score was correlated with all the section scores in the JCQ. Other ways to obtain psychosocial factors information may need to be investigated.

Previous MRI interpretations as well as participant-reported pain levels at the point of maximum severity are used as the dependent variables. Since this may have occurred anytime during the past 3 years, use of current age and BMI may not be the best approach. Age would be higher and BMI could have changed since then due to weight gains or losses. However, it is assumed that there will be only small changes that should not impact the results greatly.

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CHAPTER III

STUDY 2: MODEL BUILDING TO PREDICT LOW BACK PAIN SEVERITY IN WORKERS

3.1 Introduction

Mathematical models have been used for quite some time to predict disease or disorder risk. Several modeling strategies; ranging from simple regression models to multiple regression and logistic regression, as well as fuzzy logic and neural networks; have been used to develop injury predictive models. Low back pain (LBP) is a condition that is multifaceted involving several risk factors that may also interact. Risk factors are typically categorized into three major groups, personal, occupational and psychosocial risk factors. These factors may directly influence LBP or may interact with each other leading to LBP (Marras, 2005) (see Figure 3.1). Logistic regression models have been developed to predict the occurrence of disability associated with LBP (Cats-Baril & Frymoyer, 1991; Frymoyer, 1992a, 1992b; Frymoyer & Cats-Baril, 1987).

This study was conducted to determine how the combined effects of personal, psychosocial, and occupational factors influence the severity of LBP by generating a quantifiable model to predict LBP severity. Knowledge of how these factors impact LBP will help predict and prevent the occurrence of severe and chronic LBP. Mathematical models have been developed using only occupational, personal or psychosocial factors and few models exist that have integrated factors from each area. The predictive model

will add to the current body of knowledge and provide researchers and industry a tool to aid in predicting LBP severity, potentially preventing chronic cases and disability.

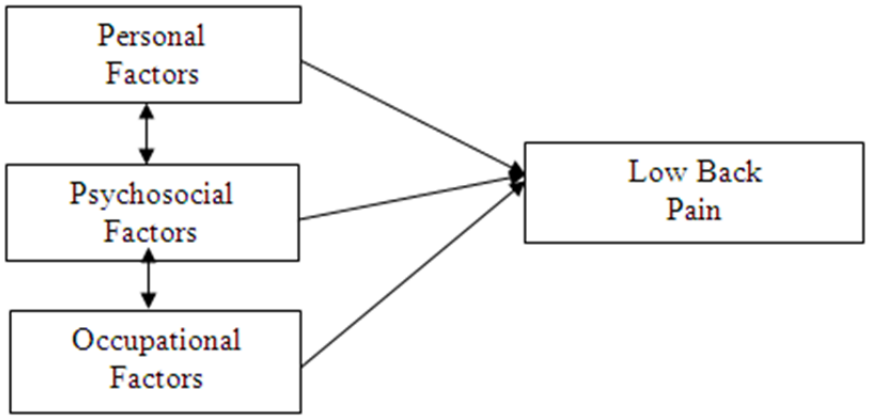

Figure 3.1 Proposed model of predictors of LBP

3.2 Literature Review

Several theoretical and mathematical models have been developed for the prediction of carpal tunnel symdrome (CTS), which is the highest reported case of WMSDs. The majority of the models consisted of only occupational risk factors (Colombini, 1998; Matias, Salvendy, & Kuczek, 1998; Moore, Wells, & Ranney, 1991; Occhipinti, Colombini, & Grieco, 1998). The effects of repetition, force and posture and their interactions were evaluated in a study to develop a mathematical prediction model to identify levels of the risk factors that contribute to CTS (Moore, et al., 1991). Some models that have also incorporated personal and psychosocial factors exist (Allie, Hoffman, Adams, & Purvis, 1998; Hales, et al., 1994; McCauley-Bell & Crumpton, 1997). Allie et. al (1998) developed a theoretical model that takes into account all risk factors contributing to WMSD development and are composed of a variety of

occupational, personal, and psychosocial risk factors. This model was based on the fact that WMSDs are multifaceted and several factors along with their interactions need to be considered in order to develop a model to predict risk.

In a study to investigate risk factors and predict CTS in fish processing operators, logistic regression models were built on personal factors and occupational factors. Though these factors were found to explain variability, it was found that a mixed model including interaction terms was more accurate and had better predictive ability than the models with only personal or occupational risk factors (Babski-Reeves & Crumpton-Young, 2003a, 2003b). A multiple regression model that included psychosocial, occupational, and personal factors as well as their interactions was developed and it was concluded that risk factor interactions have a significant impact on CTS and reporting symptoms of CTS (Babski-Reeves & Crumpton-Young, 2001).

Several model building methods exist that are used for predicting a condition. Logistic regression is used when the actual magnitude of the risk factors is to be analyzed whereas discriminant analysis is used in order to isolate the relevant risk factors. Predictive equations for CTS development using fuzzy logic were developed involving identification of risk factors, analytical hierarchy process (AHP), and risk factor qualification and quantification (McCauley-Bell & Crumpton, 1997).

Explanatory models initially developed for LBP were either mechanical/postural or behavioral/psychosocial (Klenerman, et al., 1995). As other risk factors were identified; such as personal, genetic and occupational were discovered; logistic regression models to predict LBP incorporating those risk factors were developed as well. One study conducted on health care workers found that personal factors alone explained 12% of the

risk of first-time LBP (Adams, Mannion, & Dolan, 1999). Regression models were built to study functional limitations and return to work status using personal demographic information and health history, and workplace factors in a study on LBP patients with recent onsets. Multiple regression was used to analyze functional limitations and binary logistic regression was used on the return to work variable and it was concluded that job factors were stronger predictors of LBP (Shaw, Pransky, Patterson, & Winters, 2005). Occupational factors were modeled in a follow-up study conducted on workers with no LBP initially and was found that jobs requiring large forces were at an increased risk of LBP developed later (Macfarlane, et al., 1997). Another study conducted on occupational factors included a few personal factors, though the dependent variable was signs of disc degeneration from MRI images rather than LBP reporting. This study confirmed the strong influence of occupation on LBP as well (Luoma, et al., 2000). Logistic regression models using genetic data were developed and found that whole-body vibration in addition to genetic risk factors increases the risk of LBP (Virtanen, et al., 2007). Psychosocial factors were also modelled using multiple regression and several factors were identified as risk factors for LBP as well as disability (Gatchel, Polatin, & Mayer, 1995; Kerr, et al., 2001; Schultz, et al., 2004). One study did develop a multiple logistic regression model for recurring LBP that took into account predictors from personal, psychosocial and occupational risk factors. The resultant model had high sensitivity and specificity (Marras, Ferguson, Burr, Schabo, & Maronitis, 2007).

Despite these modeling efforts, a model incorporating personal, occupational and psychosocial factors *and* their interactions has not been developed for any LBP measure. Further, mostof the models developed predict presence or absence of LBP or a spinal

abnormality. A unique contribution of this study is that the developed model is for the prediction of objective and subjective LBP severity. Like many disorders and injuries, there are levels of pain felt by current LBP sufferers and a model predicting LBP severity levels may be beneficial.

3.3 Methodology

This study built upon the data and analyses conducted in study 1. Significant factors identified in study 1 affecting the dependent variables were further evaluated here using regression techniques. For details about the risk factors, please refer to study 1. The study 1 data set was broken into two sets: a model building set and a validation set. Seventy-five percent of the data was used for model development and the remaining 25% was used for model validation. Further details are provided below.

3.3.1 Variables

Several independent variables from Study 1 were also used in Study 2. Variables and interactions from study 1 that significantly affected the pain severity measures were used as model building predictor variables for each of the dependent measures. In addition, interactions between each category (personal, psychosocial and occupational) of risk factors were also included and tested. Recall that the ODI and VAS are continuous variables, MRI severity is a polytomous variable ranging from 0 to 4, and both canal stenosis and nerve impingement were dichotomous variables classified as present (1) or absent (0). Further details on these variables are described in the methods of study 1 under section 2.3.2.

3.3.2 Data Analysis

Risk factors from the three risk factor categories were analyzed previously in study 1. These analyses identified those risk factors and risk factor interactions that significantly affected the various dependent measures and were used to build regression models to predict LBP severity measures. The general procedure was to build a predictive model for each risk factor category independently. A final predictive model that considered each risk factor category inclusively to allow for the consideration of interaction effects across categories was also built.

3.3.2.1 Model Building

Regression models were developed for each risk factor category using stepwise variable selection techniques to predict ODI, VAS, MRI severity ratings, and stenosis and impingement diagnoses scores. ODI and VAS models were developed using traditional multiple regression methods. Logistic regression was used for the remaining three dependent measures. Each model considered main effects and all two-way interactions for those factors identified as significant in study 1. The significance level to enter (SLE) = 0.100 (to include any potential factor or interaction) and the significance level to stay (SLS) = 0.100 (to remove any factors or interaction that had little predictive value) were used during the model building process.

All the personal factors were used in model building since the results of study 1 revealed that each factor significantly affected at least one severity measure as a main effect or in interaction with another personal factor. All 4 genes and interactions were used to build the gene model although only the IL-1RN gene was found to be significant (see chapter 2). This was done to see if any of the factors would be included in the model.

The occupational factors' main effects of force, posture and repetition, as well as interactions were significant (see chapter 2) and were used in model building. Vibration, though not statistically significant, was also included since there was a trend for an increase in severity ratings when participants reported exposure to vibration.

For psychosocial factors, PSS and job dissatisfaction were found to be significantly correlated with all the other factors (see chapter 2). Also, apart from PSS only job dissatisfaction, job insecurity physical and psychological demands were found to be significant as seen in the results of regression. However, the psychosocial factors model was built considering all factors to see if any of the factors would be included in the psychosocial risk factors model.

3.3.2.2 Validation

The combined model was validated. For the model building process, 5 random samples of 75% of the data were used to build the model using the procedures described above. Validation of each of the 5 models was done using the remaining 25% of the sample data. Using the predictive equations developed, the LBP severity value for each dependent variable was computed using the sampled values of the independent variables. The value obtained was compared to that originally reported by the participants and the accuracy was determined. In case of logistic regression, the sensitivity, specificity, false positives and false negatives obtained for the models were computed.

3.4 Results

3.4.1 Subjective Severity Ratings: ODI and VAS

3.4.1.1 Personal factors model

Results of the stepwise regression showed that a model with an R^2 of 0.22 (adjusted R^2 of 0.18) with the main effects of age, alcohol and smoking significantly predicted ODI ratings. No interaction effects were included in the model (Table 3.23). Smoking was included first in the model and had a partial R^2 of 0.12 i.e., smoking explained 12% of the variance. Alcohol and age both had partial R^2 of 0.05. For VAS, stepwise regression including only alcohol use and smoking were included (partial R^2 of 0.05 each) was developed (R^2 of 0.1, adjusted R^2 of 0.06) (Table 3.23).

Table 3.23 Personal factors stepwise linear regression results. Values are p-values

Independent Variable	ODI	Beta	VAS	Beta	Independent Variable	ODI	VAS
Age	**0.0634**	0.22	0.6691	-	Gender*BMI	0.4632	0.6261
Gender	0.3737	-	0.4920	-	Gender*Alcohol	0.1906	0.5545
BMI	0.7282	-	0.4542	-	Gender* FH	0.6334	0.4017
Family History (FH)	0. 5711	-	0.8268	-	Gender* PA	0.7962	0.5834
Physical Activity (PA)	0.9890	-	0.5252	-	Gender*Smoking	0.6640	0.5118
Alcohol	**0.0430**	-4.04	**0.0908**	-0.38	BMI* FH	0.4773	0.8181
Smoking	**0.0348**	-4.60	**0.0390**	-0.50	BMI* PA	0.5390	0.6156
Age*Gender	0.4743	-	0.9073	-	BMI*Alcohol	0.6569	0.7492
Age*BMI	0.9212	-	0.8821	-	BMI*Smoking	0.5839	0.6802
Age* FH	0.7182	-	0.9574	-	FH* PA	0.1494	0.9048
Age* PA	0.9959	-	0.6952	-	FH*Alcohol	0.6297	0.4210
Age*Alcohol	0.8254	-	0.9069	-	FH*Smoking	0.8444	0.5141
Age*Smoking	0.7982	-	0.5956	-	PA*Alcohol	0.9903	0.8108
Alcohol*Smoking	0.6072	-	0.5869	-	PA*Smoking	0.2130	0.1764

Note: Bolded values indicate significant differences.

3.4.1.2 Gene factors model

No models were developed considering only genetic factors.

3.4.1.3 Occupational factors model

Force and posture were included in a significant model for ODI (R^2 of 0.21, adjusted R^2 of 0.18) (Table 3.24). A significant model including only repetition was developed for VAS (R^2 of 0.06, adjusted R^2 of 0.05) (Table 3.24).

Table 3.24 Occupational factors stepwise linear regression results. Values are p-values

Independent Variable	ODI	Beta	VAS	Beta	Independent Variable	ODI	VAS
Force	**0.0285**	-4.61	0.1878	-	Force*Repetition	0.1698	0.4115
Posture	**0.0449**	-4.23	0.6672	-	Force*Vibration	0.7951	0.4660
Repetition	0.2726	-	**0.0556**	-0.42	Posture*Repetition	0.5193	0.7038
Vibration	0.5772	-	0.7850	-	Posture*Vibration	0.8529	0.9291
Force*Posture	0.1268	-	0.4836	-	Repetition*Vibration	0.6679	0.7291

Note: Bolded values indicate significant differences

3.4.1.4 Psychosocial factors model

A significant psychosocial risk factor model including only perceived stress was developed (R^2 of 0.25, adjusted R^2 of 0.23) (Table 3.25). None of the factors were included in a model to predict VAS.

Table 3.25 Psychosocial factors stepwise linear regression results. Values are p-values

Independent Variable	ODI	Beta	Independent Variable	ODI	Beta
Perceived Stress (PSS)	**<0.0001**	1.12	DL*OL	0.7565	-
Decision Latitude (DL)	0.7425	-	DL*JD	0.6455	-
Physical Demands (DPh)	0.7108	-	DL*JI	0.8951	-
Psychosocial Demands (DPs)	0.5363	-	DPh*DPs	0.8511	-
Social Support (SS)	0.3839	-	DPh*SS	0.8428	-
Organizational Level (OL)	0.8579	-	DPh*OL	0.1357	-
Job Dissatisfaction (JD)	0.9236	-	DPh*JD	0.9872	-
Job Insecurity (JI)	0.7202	-	DPh*JI	0.9552	-
PSS*DL	0.7331	-	DPs*SS	0.7337	-
PSS*DPh	0.9292	-	DPs*OL	0.8959	-
PSS*DPs	0.4951	-	DPs*JD	0.9185	-
PSS*SS	0.5604	-	DPs*JI	0.8818	-
PSS*OL	0.4901	-	SS*OL	0.6300	-
PSS*JD	0.9937	-	SS*JD	0.4564	-
PSS*JI	0.8091	-	SS*JI	0.3466	-
DL*DPh	0.8784	-	OL*JD	0.9194	-
DL*DPs	0.7818	-	OL*JI	0.7708	-
DL*SS	0.6816	-	JD*JI	0.4909	-

Note: Bolded values indicate significant differences.

3.4.1.5 Combined risk factors model

The combined model to predict ODI (considering all two-way interaction effects within and between risk factor categories) was found to have an R^2 of 0.94 and adjusted R^2 of 0.89 (Table 3.26). Several main and interaction effects were included. Eleven out of the 15 interaction effects were cross-category interactions. The personal factors: BMI and smoking, and the occupational factors: force and repetition were observed in the interactions more than the other variables. The model for VAS included the main effects of gender, alcohol consumption and smoking habits and 3 interaction terms (Table 3.26). The model had an R^2 of 0.31 and adjusted R^2 of 0.22.

Table 3.26 Final stepwise regression model results. Values are p-values

Independent Variable	ODI	Beta	VAS	Beta	Independent Variable	ODI	Beta	VAS	Beta
Gender	0.0012	4.66	0.0351	0.26	Age*Force	0.0013	-0.24	-	-
Age	<0.0001	0.19	-	-	Age*Repetition	0.0004	0.27	-	-
BMI	<0.0001	2.59	-	-	BMI*Alcohol	0.0496	3.02	-	-
Family History (FH)	0.0002	-2.46	-	-	BMI*Force	<0.0001	10.93	-	-
Physical Activity (PA)	<0.0001	-4.04	-	-	BMI*Repetition	<0.0001	5.57	-	-
Alcohol	0.0023	-3.18	0.0827	0.16	BMI*Vibration	<0.0001	-16.32	-	-
Smoking	<0.0001	-1.32	0.0005	-1.20	FH*PA	0.0001	5.12	-	-
Posture	<0.0001	0.15	-	-	FH*Repetition	0.0899	1.88	-	-
Force	<0.0001	4.98	-	-	PA*Smoking	<0.0001	8.11	-	-
Repetition	<0.0001	3.06	-	-	PA*Force	<0.0001	-7.22	-	-
Vibration	<0.0001	-14.69	0.0045	-0.39	Alcohol*Vibration	-	-	0.0478	0.61
Perceived Stress (PSS)	<0.0001	-0.27	-	-	Smoking*Posture	<0.0001	-5.69	-	-
Gender*Alcohol	0.0052	2.80	-	-	Smoking*Repetition	0.0076	-3.19	-	-
Gender*PSS	0.0040	0.54	-	-	Smoking*Vibration	-	-	0.0008	-1.17
Gender*Smoking	-	-	0.0108	0.67	Vibration*PSS	<0.0001	1.18	-	-

Note: Only significant factors are shown in the table

3.4.2 Physician Ratings: MRI Severity, Stenosis and Impingement

3.4.2.1 Personal factors model

Only age was found to significant predict MRI severity ratings ($R^2 = 0.12$, coefficient = 0.06). Family history was the only significant predictor of nerve impingement (R^2=0.08, coefficient = 0.74). No predictive model for stenosis was found.

3.4.2.2 Gene, Occupational, and Psychosocial factor models

No models were found for any of the MRI variables for each of these risk factor categories (genes, occupational, and psychosocial risk factors).

3.4.2.3 Combined risk factors model

A significant model with PSS, age, repetition, IL-1RN, and the interaction effect of age and repetition as predictor variables of MRI severity was obtained with an R^2 of 0.44 (Table 3.27). Family history of LBP was the only factor included in the final model to predict nerve impingement (R^2= 0.09, coefficient = 0.74) which was same as the personal factors model. None of the factors significantly predicted stenosis.

Table 3.27 Combined model for MRI severity

Independent Variable	P-value	Coefficient
Age	0.0282	0.10
PSS	0.0181	-0.31
Repetition	0.1845	2.71
Il-1RN	0.0265	-3.06
Age*Repetition	0.0524	-0.10

3.4.3 Validation

3.4.3.1 Validation for ODI ratings

Stepwise regression models built from 5 random samples of 75% of the data (45 participants) resulted in different models when compared to the model of the full sample (all 60 participants) presented above (Table 3.28). Full model accuracy was found to be 91.4% (adj. R^2 = 0.89). Model accuracy of the 5 sample models using the remaining 25% of the data were found to be 61.6% for sample 1 (adj. R^2 0.77), 59.7% for sample 2 (adj. R^2 0.79), 71.2% for sample 3 (adj. R^2 0.59), 65.8% for sample 4 (adj. R^2 0.46) and 15.4%

for sample 5 (adj. R^2 0.99). Only vibration, PSS and the interaction effect of vibration and PSS were present in all the models.

Table 3.28 Variables included in the model to predict ODI

Independent Variable	Full Sample	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5
Gender	X					X
Age	X	X			X	X
BMI	X		X			X
History	X	X	X	X		X
Physical activity	X	X	X	X		X
Alcohol	X		X	X	X	X
Smoking	X		X			X
Posture	X	X				X
Force	X	X	X	X		X
Repetition	X					X
Vibration	X	X	X	X	X	X
PSS	X	X	X	X	X	X
*Gender *PSS*	X					X
*Age*Force*	X					
*Age*Repetition*	X					X
*Age*Vibration*		X				
Age PSS*		X				
*BMI*Force*	X		X			X
*BMI*Repetition*	X					X
*BMI*Vibration*	X		X			
*BMI*PSS*						X
*History*Force*		X				X
*History*Repetition*	X					
*History*Vibration*				X		
*History*PSS*						X
*Physical Activity*Force*	X		X	X		
*Physical Activity*PSS*		X				
*Alcohol*Post*						X
*Alcohol*Force*						X
*Alcohol*Repetition*						X
*Smoking*Posture*	X					
*Smoking*Force*			X			
*Smoking*Repetition*	X					X

Table 3.28 (continued)

Independent Variable	Full Sample	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5
*Posture*PSS*		X				
*Vibration*PSS*	X	X	X	X	X	X
*Gender *Age*						X
*Gender *BMI*						X
*Gender *Physical Activity*						X
*Gender *Alcohol*	X					
*Age*Physical Activity*						X
*BMI*History*						X
*BMI*Alcohol*	X		X			X
*History*Physical Activity*	X		X	X		
*History*Alcohol*			X			X
*Physical Activity*Smoking*	X		X			
*Alcohol*Smoking*						X

3.4.3.2 Validation for VAS ratings

As with ODI, the full sample model differed significantly from the 5 models developed using 75% of the data (Table 3.29). Model accuracy of the full sample model was found to be 83.4% (adj. $R^2 = 0.22$). Model accuracy for the newly developed models were found to be 80.2% for sample 2 (adj. R^2 0.05), 73.44% for sample 3 (adj. R^2 0.21) and 68.52% for sample 4 (adj. R^2 0.57). Sample 1 and sample 5 did not result in a model with predictors of VAS. None of the variables were common in all models

Table 3.29 Variables included in the model to predict VAS

Independent Variable	Full Sample	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5
Gender	X				X	
BMI					X	
History					X	
Alcohol	X		X			
Smoking	X			X	X	
Repetition				X	X	
Vibration					X	
PSS	X				X	
*Gender *Smoking*	X					
*Alcohol*Vibration*	X					
*Smoking*Vibration*	X					
*Smoking*Repetition*				X		
*Gender *BMI*					X	
*Gender *Smoking*					X	
*BMI*Smoking*					X	
*BMI*Repetition*					X	
*Repetition*PSS*					X	
*Vibration*PSS*					X	

3.4.3.3 Validation for MRI ratings

Although the logistic regression model for the full sample resulted in a model with 5 factors, stepwise logistic regression models run with 5 random samples of 75% of the data (27 participants) resulted in models with only age as a predictor variable and in only 2 out of the 5 samples (Table 3.30). Sample 1, 3 and 5 did not result in a predictive model. Accuracy measures in terms of percent concordant and percent discordant are give in table 3.31.

Table 3.30 Variables included in the model for MRI severity

Independent Variable	Full Sample	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5
Age	x		x		x	
PSS	x					
Repetition	x					
Il-1RN	x					
*Age*Repetition*	x					

Table 3.31 Accuracy measures for MRI severity prediction

Sample	Percent Concordant	Percent Discordant	Percent Tied
Full sample	88.6	10.5	1.0
Sample 2	69.3	29.2	1.5
Predicted Sample 2	64.3	28.6	7.1
Sample 4	70.3	27.7	1.9
Predicted Sample 4	87.5	12.5	0.0

Stepwise logistic regression models run for impingement on 5 random samples with 75% of the data (27 participants) resulted in a model with only family history of LBP as a predictor variable in 2 of the 5 samples as well as the full sample (Table 3.32). Sample 2, 4 and 5 did not result in a predictive model. Accuracy measures for the samples at a cutoff probability of 0.32 are given in table 3.33.

Table 3.32 Variables included in the model for MRI impingement

Independent Variable	Full Sample	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5
Family History	X	X		X		

Table 3.33 Accuracy measures for nerve impingement prediction

Sample	Sensitivity	Specificity	False Positive	False Negative
Full sample	55.5%	77.8%	54.5%	16%
Sample 1	50%	85.7%	50%	14.3%
Predicted Sample 1	66.7%	50%	60%	25%
Sample 3	66.7%	81%	50%	10.5%
Predicted Sample 3	33.3%	66.7%	66.7%	33.3%

3.5 Discussion

Personal, occupational and psychosocial factors were found to be significant predictors of LBP severity ratings. More importantly, predicting severity ratings was significantly improved when considering interaction effects both within and across risk factor categories (94% of variance explained for ODI and 31% for VAS). When considering risk factor categories individually, in case of ODI, the psychosocial risk factor model was found to provide the most adequate model (explaining 25% of the variance in the data), followed by a personal risk factor model (22% of variance explained), with an occupational risk factor model being the least adequate model (21% of variance explained). No model for the genetic factors was obtained. In case of VAS, no models were obtained for genetic and psychosocial factors. Personal factors explained 10% and occupational factors explained 6% of the variance. Although the individual risk factor models consisted of only main effects, it was seen that the combined risk factor model included several within category and cross-category interactions in addition to the main effects in predicting severity. In the combined factors model for ODI, the first factor

to enter was a cross-category interaction effect that explained 32% of the variance. In fact, 60% of the variance was explained by cross-category interactions in total. For VAS, 21% out of the 31% of variance explained by the factors studied here were of cross-category interactions. These findings support previous literature that found a causal relationship between combinations of risk factors and LBP (Marras, 2005).

In addition to some expected findings, some unexpected findings were also obtained. Though expected, the VAS ratings were not well explained by the factors studied here. A reason for this could be that participants were asked to rate the worst pain felt by the in their low back and most participants marked worst imaginable on the scale which could have led to a ceiling effect. It was also observed that the elderly tended to mark their worst pain much lower. This could be due to increased pain tolerance or reduced pain perception (Dionne et al., 2006). Since VAS and ODI are measuring different things, it may be possible that the factors studied here are more useful for predicting ODI than VAS. Also, the ODI is a condition-specific measure and is more sensitive to changes in individuals with the specific condition (Khorsan, et al., 2008).

An occupational factors model or genetic factors model was not obtained for the MRI ratings. Since occupational factors are thought to be directly linked to spine abnormalities, it was expected that at least one occupational factor would be helpful in predicting the MRI ratings, stenosis or impingement. A previous study of risk factors on disc degeneration based on MRI showed that occupational loading was related to disc degeneration as seen as a result of logistic regression (Luoma et al., 2000). A longitudinal study conducted to predict the onset of LBP found that occupational factors; such as lifting, pulling, pushing, and prolonged standing/walking; increased the risk of a

new episode of LBP (Macfarlane, 1997). A case-control study on risk factors for new episode of LBP also showed the presence of occupational factors in a logistic regression model in addition to psychosocial risk factors (Kerr et al., 2001). These findings are in contrast to the findings of this study and could be due to the fact that occupational factors may affect the onset of LBP to a greater extent when compared to its effects on severity. Two studies that developed logistic regression models taking into account personal, occupational and psychosocial factors, but one for chronicity (Fransen et al., 2002) and the other for recurrence (Marras et al., 2007) showed the presence of risk factors from all 3 categories in the combined model.

The main mechanism by which genetic factors could influence LBP is through changes in the biomechanical properties of the spine and was expected to predict severity based on MRI measures. Although none of the genetic, occupational and psychosocial factors were significant predictors in their respective categories, when the IL-1RN was included in the combined risk factors model for MRI severity, a significant model with 1 factor from each of the categories was obtained. This may be because the genetic factors may not influence LBP severity by itself but in the presence of other factors which in this case include personal, psychosocial and occupational factors. This finding again shows that studying each risk factor category in isolation may not be enough to determine the effects on LBP.

Validations were conducted on 5 random samples and showed that for ODI only 4 out of the 5 had an accuracy of greater than 60%. In case of VAS, 2 samples did not result in a model and the other 3 had accuracies above 60%. Based on this it can be said that the practicality of the models in the present form may be questionable as the

validations show that the models obtained were not consistent and with varying accuracies. The study may have to be replicated with a larger sample including patients and healthy participants.

The sample size in the study was considered a limitation and a post hoc power analysis was done using G*Power 3.1 (Erdfelder, Faul, & Buchner, 1996), a general power analysis program, to calculate the power of the tests used in the study. The power was calculated for a sample size of 60, a significance level of 0.1 and the effect size calculated from the outputs that ranged between 0.2 to 0.3 for ODI and MRI severity, and 0.05 to 0.1 for VAS. The power for the tests is given in the table 3.34.

Table 3.34 Calculated power values

	Personal	Genetic	Occupational	Psychosocial	Combined
ODI	0.96	-	0.97	0.99	1
VAS	0.74	-	0.63	-	0.98
MRI	0.71	0.85	-	0.99	1

In case of the gene effects for ODI and VAS, the effect size was found to be very small (about 0.01). The sample size required to see significant effects was calculated to be about 378 for ODI, 92 for VAS and 50 for MRI severity. Therefore in case of gene effects, a reason that no significance was found could be related to the sample size.

A sample size of 60 was chosen based on sample size estimates to obtain a power of 70 for a two-tailed test, using a level of significance value as 0.05 and an effect size of

0.4 (Cohen, 1988). Participants were paid $50 to participate which was $3000 in recruitment costs. Doubling the sample size to 120 would double the cost but would not reach even half of the required sample size for ODI (378). Also, the cost of the DNA analysis for the 60 participants was at $7000 which was at the higher end for a pilot project such as this. In terms of time, data collection for 60 participants lasted about a year. If data collection continued at the same pace, it would have taken about 6 years to complete data collection alone which would have not been feasible.

The use of genetic data by itself may not be useful as a predictor of risk since disorders are usually the complex interplay of multiple factors. Physicians have been ordering genetic tests or referring patients to genetic testing centers for a number of diseases/disorders currently (Shields et al., 2008) but the prognostic value of genetic data is still questionable (Norrgard, 2008; Pray, 2008). This is true in cases of diseases where for one, knowing that you are at a risk of fatal disease cannot help you in any way, and second knowing that you have the gene that has been associated with a disorder but don't know what to do with the information. The second case relates to LBP where the presence of a gene polymorphism may indicate risk. In this case, genetic information in addition to other factors may help us have a better understanding of the risk the person is under and hence, help in designing better risk reduction strategies. This information may also be useful in job placements where if a potential employee is found to be at a risk of developing severe, disabling LBP, they can be advised not to take the job or if they take the job to employ suitable risk reduction strategies.

It is feared that the use of genetic information may be used against employees during hiring, workman compensation cases, etc., and as a result, individuals may avoid

or refuse to submit to genetic testing. In 2008, a law was passed in the USA known as the Genetic Information Nondiscrimination Act (GINA) that protects Americans against such discrimination. Several years down the line, when genetic testing becomes a routine procedure and when its importance becomes familiar, it is expected that more of such acts that protect patients will be in place. This information can then be used in risk factor models to predict risk of non-fatal but disabling disorders such as LBP.

3.6 Limitations

It is assumed that all possible risk factors have been included in the study. This assumption is based on research conducted on the risk factors and the possible contribution of each factor on the etiology and progression of LBP. Other risk factors that have not been discovered may exist that would explain variability not explained by the factors included in this study. Since most of the data was obtained through questionnaires, there may be some impact of self report data on the findings. Subjective data may not be accurate as participants may willingly or unwillingly hide some facts or exaggerate/overplay actual facts. Another problem associated with the data especially in this study is 'recall bias'. The participants were people who had back pain over the past year and were asked to report their maximum pain severity level. Therefore, the information recalled by the participants in answering the questions may not be very accurate. However, it is expected that the model developed with the available data is fairly predictive but needs to be further validated.

Another limitation may be the use of the non-traditional alpha value of 0.1 instead of 0.05 for all analyses. This alpha value was chosen since this is an exploratory study with a relatively small sample size and because of the need to be able to identify all

significant effects. Further, the p-values have been provided for all analysis that provides the reader with a value that can be used to according to their own judgment. A 0.05 could have been used in chapter 2 and this would have resulted in the elimination of only a few effects that were considered significant at the 0.1 level. However, to maintain consistency in chapter 3, where the significance level for entry and removal was set for 0.1, the 0.1 alpha level was used throughout. Stepwise regression was run setting the alpha levels at 0.05 but this failed to identify effects that could be of importance for the model building.

The MRI ratings used in this study were only from 36 participants that were available and was used in analysis and reported. This sample size may be too small to generalize the results and further studies with larger sample sizes may be warranted especially to study severity based on MRI measures. Further, loss of genetic data due to technical failures during DNA processing and sequencing was not taken into account which resulted in an even smaller sample. This problem may have to be considered when designing future studies.

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CHAPTER IV

CONCLUSION

The study attempted to develop a model that could predict severity levels of occupational low back pain. With this, the aim of developing a preventive method for chronic and severe back pain for those in physically demanding jobs can be achieved in the future. In the long run, this will help the industrial economy by saving millions of dollars in compensations and lost work days.

To our knowledge this is the first study that investigated the effects of various personal, occupational and psychosocial factors and interactions on LBP severity levels. Predicting the severity level of LBP may be beneficial in the current situation with a large percentage of the adult population reporting some form of LBP during their lifetime. This is also the first study to investigate associations between previously identified genes polymorphisms and LBP severity levels.

In general, the results from this research supports the hypothesis that interaction effects across the different risk factor categories significantly affect LBP severity and could be useful in predicting the risk of severe LBP. Additional research including healthy participants and a larger sample size may be needed. Further, the use of direct measures of occupational risk factors obtained from assessments of actual job tasks may help improve the accuracy of the data collected.

APPENDIX A

IRB APPROVAL

Compliance Division
Administrative Offices
Animal Care and Use (IACUC)
Human Research Protection Program (IRB)
1207 Hwy 182 West, Suite C
Starkville, MS 39759
(662) 325-3496 - fax

Safety Division
Biosafety (IBC)
Radiation Safety
Hazardous Waste
Chemical & Lab Safety
Fire & Life Safety
70 Morgan Avenue
Mississippi State, MS 39762
(662) 325-8776 - fax

http://www.orc.msstate.edu
compliance@research.msstate.edu
(662) 325-3294

MISSISSIPPI STATE UNIVERSITY

December 16, 2010

Keerthi Govindu
Industrial and Systems Engineering
Mail Stop 9542

RE: IRB Study #10-282: Roles of Genes in Occupational Low Back Pain

Dear Ms. Govindu:

The above referenced project was reviewed and approved via expedited review for a period of 12/16/2010 through 12/15/2011 in accordance with 45 CFR 46.110 #2, 5, & 7. Please note the expiration date for approval of this project is 12/15/2011. If additional time is needed to complete the project, you will need to submit a Continuing Review Request form 30 days prior to the date of expiration. Any modifications made to this project must be submitted for approval prior to implementation. Forms for both Continuing Review and Modifications are located on our website at http://www.orc.msstate.edu.

Any failure to adhere to the approved protocol could result in suspension or termination of your project. Please note that the IRB reserves the right, at anytime, to observe you and any associated researchers as they conduct the project and audit research records associated with this project.

You must use copies of the stamped consent form for obtaining consent from participants.

Please refer to your docket number (#10-282) when contacting our office regarding this project.

We wish you the very best of luck in your research and look forward to working with you again. If you have questions or concerns, please contact Jonathan Miller at jmiller@research.msstate.edu or call 662-325-2238.

Sincerely,

Jonathan Miller, CIP
IRB Officer and Assistant Director

cc: Kari Reeves
SPA

APPENDIX B

INFORMED CONSENT

Mississippi State University
Informed Consent Form for Participation in Research

Title of Research Study: Role of Genes in Occupational Low Back Pain

Study Site: Longest Student Health Center, MSU and Human Systems Engineering Laboratory (McCain 300), Department of Industrial and Systems Engineering, MSU

Researchers: Nirathi Keerthi Govindu, Mississippi State University; Dr. Kari Babski-Reeves, Mississippi State University.

Purpose

The purpose of this research study is to test and confirm the role of genes in occupational low back pain.

Procedures

If you are at least 18 years of age, not pregnant, and currently suffer from back pain as a result of your current occupation, you will be asked to meet with the researcher at the Longest Student Health Center at MSU and complete informed consent documents. The informed consent document will also contain a section where authorization for disclosure of protected health information (PHI) will be obtained. This authorization is required for the physician to release your pain severity ratings based on MRI readings. On obtaining authorization, the signed form will be taken back to the physician as proof to obtain the required medical information

After completing the informed consent process, you will be asked to complete a short questionnaire that includes basic information about you (e.g., age, gender, race, height, weight, personal habits etc.). You will also be asked to complete a couple of surveys to understand your pain level and other information. A blood sample of 5ml (about a teaspoon) will be collected from you by a medical technician at the Health Center using clinical procedures. Blood will be drawn from the arm using a vacutainer system (consisting of a needle and tube). All this will be completed within an hour. The blood will be stored in code-labeled tubes, which will not be linked to your identity, containing an anti-coagulant and stored in a freezer. The blood samples collected will be sent to an outside lab and will be used only for this research study. The blood samples are required in order to study genes that are thought to be involved on low back pain.

Risks or Discomforts

Risks are minimum and are no greater than the minimum risk associated with the needle/syringe technique of obtaining a blood sample. You may experience some pain due to drawing of blood but can be assured that certified professionals at the health center will be carrying out the procedure. Some of the information asked for may involve social risks. The information in questionnaires will not be linked to your identity in any way and will only be available to researchers. You may choose not to answer questions that may appear to put you at any sort of risk.

Benefits
There is no direct benefit associated with your participation. The data collected may provide evidence to support the hypothesis that genes do contribute or predispose workers to greater risks of MSDs.

Incentive to participate
You will be compensated monetarily with $50.

.

Confidentiality
Individual identities will be protected and will not in any way be connected with any written summary of results that may later be published. At no time will your name be collected on any data collection forms.

Please note that these records will be held by a state entity and therefore are subject to disclosure if required by law.

Disclosure of Protected Health Information (PHI) Authorization
Protected Health Information (PHI) is health information that indentifies you. PHI is protected by federal law under HIPAA (Health Insurance Portability and Accountability Act). To take part in this research you must give the research team permission to have access to an interpretation of your MRI image made by the orthopedic surgeon in order to establish injury severity. All identity will be removed from all data and your associated participant number will be used. Individual identities will be protected and will not in any way be connected with any written summary of results that may later be published. All consent forms will be securely stored in a locked office and will be stored separately from any data files. General information about you (height, weight, age, gender, etc.), and injury history (recent or past injuries) will not be linked to your identity and will only be linked to the data files through an arbitrary subject identifier.
Please sign below to authorize the disclosure of your MRI information by the Starkville Orthopedic Clinic.

I request and authorize the Starkville Orthopedic Clinic to disclose my protected health information to the researchers as described above.

_____ _____
Participant Signature Date

Questions
If you have any questions about this research project, please feel free to contact Nirathi Keerthi Govindu at 727-415-4692.

For further information please contact: Kari Babski-Reeves, Department of Industrial and Systems Engineering, Mississippi State University, Starkville, MS 39759 (662) 325-1677, kari@ise.msstate.edu

For questions regarding your rights as a research participant, or to express concerns or complaints, please feel free to contact the MSU Regulatory Compliance Office by phone at 662-325-3994, by e-mail at irb@research.msstate.edu, or on the web at http://orc.msstate.edu/*participant/*.

Voluntary Participation

Please understand that your participation in this study is voluntary. You are free to refuse to participate, decline to answer any question, or withdraw from this study at any time for any reason. Your refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled. You may discontinue your participation at any time without penalty or loss of benefits.

Approval of this Research

The research project has been approved by the Institutional Review Board at Mississippi State University for projects involving human participants. The IRB approval number is 10-282.

Please take all the time you need to read through this document and decide whether you would like to participate in this research study.

If you agree to participate in this research study, please sign below. You will be given a copy of this form for your records.

_____ _____

Participant Signature

_____

Investigator Signature Date

APPENDIX C

PARTICIPANT DEMOGRAPHIC QUESTIONNAIRE

Participant Demographics

Participant #: _____ Date: _____

Age: _____

Gender: ☐ Male ☐ Female

Height (in): _____ Weight (lb): _____

Ethnicity:
☐ African American/Black
☐ Asian
☐ Asian American
☐ Caucasian
☐ Hispanic/Latino
☐ Native American
☐ Other: _____

Family History of Low Back pain? ☐ Yes ☐ No

Physical Activity Level:
☐ Less than 3 times a week (short workouts of about 30 minutes)
☐Less than 3 times a week (workouts lasting an hour or more)
☐ 3 to 5 times a week (short workouts of about 30 minutes)
☐3 to 5 times a week (workouts lasting an hour or more)
☐ More than 5 times a week (short workouts of about 30 minutes)
☐ More than 5 times a week (workouts lasting an hour or more)

Alcohol Consumption:
☐ Abstainers
☐ Light – 3 drinks per week
☐ Moderate – 4 to 14 drinks (men) and 4 to 7 (women)
☐ Heavy – more than 14 drinks (men) and more than 7 (women)

Smoking Habits:

☐ None
☐ Less than 5 a day
☐ 5 to 10 a day
☐ 10 to 15 a day
☐ More than 15 a day

Work History:

Are you currently employed? ☐ Yes ☐ No

If yes, what is your current occupation and job title? How long have you been employed? _____

How many hours a day do you work? _____ Hours

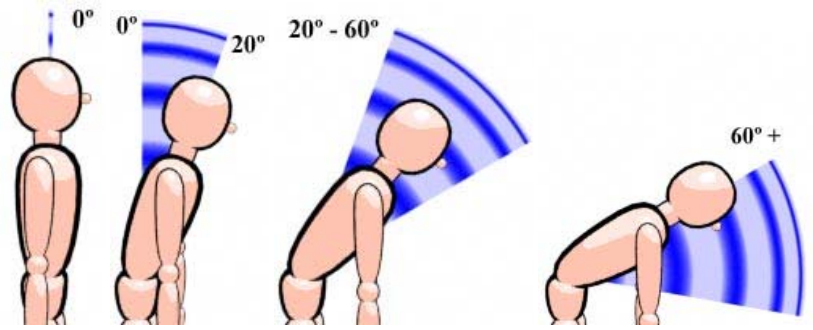
Do you do the same job everyday or rotate: ☐ Yes ☐ No

If yes, what job do you rotate to and for how many hours? _____

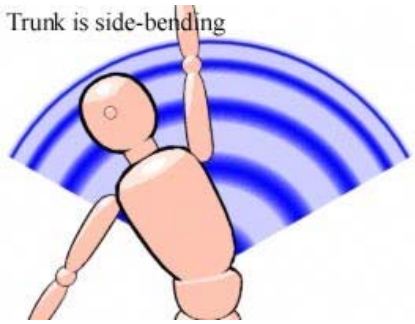
What do you think is the primary cause of your injury? _____

POSTURE:

- What was your most assumed back posture while working? (Mark one)



- Was side bending or twisting involved? (Mark all that apply)



How long was the posture assumed? ☐ ≥ 8hrs ☐ 4 – 8hrs ☐ 2 -4 hrs ☐ < 2hrs

FORCE:

Did your job involve (Mark one)
- ☐ Less than 4.4lbs of intermittent force/load?
- ☐ 4.4 to 22lbs of intermittent force/load?
- ☐ 4.4 to 22lbs of static/repeated force/load?
- ☐ 22lbs or more intermittent force/load?
- ☐ 22lbs or more of static/repeated force/load?

How long was it required? ☐ ≥ 8hrs ☐ 4 – 8hrs ☐ 2 -4 hrs ☐ < 2hrs

REPETITION:

Did your job involve repetition with a cycle time of (Mark one)
- ☐ Less than 30 seconds?
- ☐ 30 seconds to 1 minute?
- ☐ Greater than 1 minute?

How long was it required? ☐ ≥ 8hrs ☐ 4 – 8hrs ☐ 2 -4 hrs ☐ < 2hrs

VIBRATION:

Did your job involve activities that subject you to whole body vibration (for example driving)? ☐ Yes ☐ No

How long was it required? ☐ ≥ 8hrs ☐ 4 – 8hrs ☐ 2 -4 hrs ☐ < 2hrs

APPENDIX D

PERCEIVED STRESS QUESTIONNAIRE

INSTRUCTIONS: The questions in this scale ask you about your feelings and thoughts during THE LAST MONTH. In each case, you will be asked to indicate your response by placing an "X" over the circle representing HOW OFTEN you felt or thought a certain way. Although some of the questions are similar, there are differences between them and you should treat each one as a separate question. The best approach is to answer fairly quickly. That is, don't try to count up the number of times you felt a particular way, but rather indicate the alternative that seems like a reasonable estimate.

	Never	Almost Never	Fairly Sometimes	Often	Very Often
1. How often have you been upset because of something that happened unexpectedly?	☐	☐	☐	☐	☐
2. How often have you felt that you were unable to control the important things in your life?	☐	☐	☐	☐	☐
3. How often have you felt nervous and "stressed"?	☐	☐	☐	☐	☐
4. How often have you dealt successfully with day to day problems and annoyances?	☐	☐	☐	☐	☐
5. How often have you felt that you were effectively coping with important changes that were occurring in your life?	☐	☐	☐	☐	☐
6. How often have you felt confident about your ability to handle your personal problems?	☐	☐	☐	☐	☐

7. How often have you felt that things were going your way?	☐	☐	☐	☐	☐
8. How often have you found that you could not cope with all the things that you had to do?	☐	☐	☐	☐	☐
9. How often have you been able to control irritations in your life?	☐	☐	☐	☐	☐
10. How often have you felt that you were on top of things?	☐	☐	☐	☐	☐
11. How often have you been angered because of things that happened that were outside of your control?	☐	☐	☐	☐	☐
12. How often have you found yourself thinking about things that you have to accomplish?	☐	☐	☐	☐	☐
13. How often have you been able to control the way you spend your time?	☐	☐	☐	☐	☐
14. How often have you felt difficulties were piling up so high that you could not overcome them?	☐	☐	☐	☐	☐

References:

- Cohen, S., Kamarck, T., and Mermelstein, R. (1983). A global measure of perceived stress. *Journal of Health and Social Behavior, 24,* 386-396.

- Cohen, S. and Williamson, G. Perceived Stress in a Probability Sample of the United States. Spacapan, S. and Oskamp, S. (Eds.) *The Social Psychology of Health.* Newbury Park, CA: Sage, 1

APPENDIX E

JOB CONTENT QUESTIONNAIRE

Instructions: Please answer each question by checking off the one answer that best fits your job situation. Sometimes none of the answers fits exactly. Please choose the answer that comes closest.

1. What is your education? (Highest grade completed)

☐ Elementary School
☐ Junior High (8th and 9th grade)
☐ High School
☐ Junior College (1-2 yrs College)
☐ College Graduate
☐ Graduate School

2. What level of skill is required on your job in terms of years of formal training? (not necessarily the same as your education)

☐ Elementary education only (6)
☐ Junior high school education (9)
☐ High school graduate (12)
☐ Some college education (14)
☐ College Graduate (4-year) (16)
☐ Graduate School (18)

3. My job requires that I learn new things.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

4. My job involves a lot of repetitive work.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

5. My job requires me to be creative.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

6. My job allows me to make a lot of decisions on my own.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

7. My job requires a high level of skill.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

8. On my job, I have very little freedom to decide how I do my work.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

9. I get to do a variety of different things on my job.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

10. I have a lot to say about what happens on my job.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

11. I have an opportunity to develop my own special abilities.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

12. My job requires working very fast.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

13. My job requires working very hard.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

14. My job requires lots of physical effort.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

15. I am not asked to do an excessive amount of work.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

16. I have enough time to get the job done.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

17. I am often requires to move or lift very heavy loads on my job.

18. My work requires rapid and continuous physical activity.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree
☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

19. I am free from conflicting demands that others make.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

20. My job requires long periods of intense concentration on the task.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

21. My tasks are often interrupted before they can be completed, requiring attention at a later time.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

22. My job is very hectic.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

23. I am often required to work for long periods with my body in physically awkward positions.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

24. I am often required to work for long periods with my head and arms in physically awkward positions.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

25. Waiting on work from other people or departments often slows me down on my job.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

26. How steady is you work? (check one)

☐ Regular and steady ☐ Seasonal ☐ Frequent layoffs ☐ Both seasonal and frequent layoffs ☐ Other

27. My job security is good.

☐ Strongly Disagree ☐ Disagree ☐ Agree ☐ Strongly Agree

28. During the past year, how often were you in a situation where you faced job loss or layoff.

☐ Never ☐ Faced the possibility once ☐Faced the possibility more than once ☐ Constantly ☐ Actually layed off

29. Sometimes people permanently lose jobs they want to keep. How likely is it that during the next couple of years you will lose your present job with your employer.

☐ Not at all likely ☐ Not too likely ☐ Somewhat likely ☐ Very likely

30. How satisfied are you with your job?

☐ Not at all ☐ Not too ☐ Somewhat ☐ Very

31. Would you advise a friend to take this job?

☐ Advise against ☐ Have doubts about it ☐ Strongly recommend

32. Would you take this job again?

☐ Take without hesitation ☐ Have second thoughts ☐ Definitely not

33. How likely is it that you will find a new job in the next year?

☐ Very likely ☐ Somewhat ☐ Not at all

34. Is this job like what you wanted when you applied for it?

☐ Very much ☐ Somewhat like ☐ Not very much like

Reference:

Karasek, R. A., Brisson, C., Kawakami, N., Houtman, I., & Bongers, P. M. (1998). The Job Content Questionnaire (JCQ): An instrument for internationally comparative assessments of psychosocial job characteristics. *Journal of Occupational Health Psychology, 3*, 322-355.

APPENDIX F

PAIN SEVERITY QUESTIONNAIRE

MODIFIED OSWESTRY LOW BACK PAIN DISABILITY INDEX (ODI)

Purpose: The ODI is a disease-specific disability measure is used to establish a level of disability, stage a patient's acuity status, and monitor change over time.

Scoring:

The ODI is made up of 10 questions. Each question is scored from 0-5 (minimum to maximum).

EXAMPLE:
Pain Intensity
_____The pain is mild and comes and goes. *(A check at this level is scored as 0)*
_____The pain is mild and does not vary much. *(A check at this level is scored as 1)*
_____The pain is moderate and comes and goes. *(A check at this level is scored as 2)*
_____The pain is moderate and does not vary much. *(A check at this level is scored as 3)*
_____The pain is severe and comes and goes. *(A check at this level is scored as 4)*
_____The pain is severe and does not vary much. *(A check at this level is scored as 5)*

2. The point total from each section is summed and the then divided by the total number of questions answered and multiplied by 100 to create a percentage disability. The scores range from 0-100% with lower scores meaning less disability.

ODI = (Sum of items scored/Sum of sections answered) X 100

3. Typically all items are filled out so you can just add up the score from each section and double it to get the final percentage score.

Measurement Characteristics: The measurement characteristics of the ODI are good to excellent. Test-Retest ICC (2,1) 0.83 - 0.94 (1-14 days)2 and 0.90 over 4 weeks in a group of patients judged stable.3 The minimal clinically important difference for the Oswestry is 8 – 12 percentage points.2

References:

1. Delitto A, Erhard RE, Bowling RW. A treatment-based classification approach to low back syndrome: identifying and staging patients for conservative management. Phys.Ther. 1995; 75:470-489.
2. Fritz JM, Irrgang JJ. A Comparison of a Modified Oswestry Disability Questionnaire and the Quebec Back Pain Disability Scale. Phys Ther 2001; 81:776-788.
3. Kopec JA, Esdaile JM. Spine Update. Functional disability scales for back pain. Spine 1995; 20:1943-1949.

Instructions:
This questionnaire has been chosen to allow the researcher to get a subjective rating of the level of low back pain experienced by you. Please answer every question by placing a mark on the line that best describes your condition.

Pain Intensity

_____The pain is mild and comes and goes.
_____The pain is mild and does not vary much.
_____The pain is moderate and comes and goes.
_____The pain is moderate and does not vary much.
_____The pain is severe and comes and goes.
_____The pain is severe and does not vary much.

Personal Care (Washing, Dressing, etc.)

_____I do not have to change the way I wash and dress myself to avoid pain.
_____I do not normally change the way I wash or dress myself even though it causes some pain.
_____Washing and dressing increases my pain, but I can do it without changing my way of doing it.
_____Washing and dressing increases my pain, and I find it necessary to change the way I do it.
_____Because of my pain I am partially unable to wash and dress without help.
_____Because of my pain I am completely unable to wash or dress without help.

Lifting

_____I can lift heavy weights without increased pain.
_____I can lift heavy weights but it causes increased pain
_____Pain prevents me from lifting heavy weights off of the floor, but I can manage if they are conveniently positioned (ex. on a table, etc.).
_____Pain prevents me from lifting heavy weights off of the floor, but I can manage light to medium weights if they are conveniently positioned.
_____I can lift only very light weights.
_____I cannot lift or carry anything at all.

Walking

_____I have no pain when walking.
_____I have pain when walking, but I can still walk my required normal distances.
_____Pain prevents me from walking long distances.
_____Pain prevents me from walking intermediate distances.
_____Pain prevents me from walking even short distances.
_____Pain prevents me from walking at all.

Sitting

_____Sitting does not cause me any pain.
_____I can only sit as long as I like providing that I have my choice of seating surfaces.
_____Pain prevents me from sitting for more than 1 hour.

_____Pain prevents me from sitting for more than 1/2 hour.
_____Pain prevents me from sitting for more than 10 minutes.
_____Pain prevents me from sitting at all.

Standing
_____I can stand as long as I want without increased pain.
_____I can stand as long as I want but my pain increases with time.
_____Pain prevents me from standing more than 1 hour.
_____Pain prevents me from standing more than 1/2 hour.
_____Pain prevents me from standing more than 10 minutes.
_____I avoid standing because it increases my pain right away.

Sleeping
_____I get no pain when I am in bed.
_____I get pain in bed, but it does not prevent me from sleeping well.
_____Because of my pain, my sleep is only 3/4 of my normal amount.
_____Because of my pain, my sleep is only 1/2 of my normal amount.
_____Because of my pain, my sleep is only 1/4 of my normal amount.
_____Pain prevents me from sleeping at all.

Social Life
_____My social life is normal and does not increase my pain.
_____My social life is normal, but it increases my level of pain.
_____Pain prevents me from participating in more energetic activities (ex. sports, dancing, etc.)
_____Pain prevents me from going out very often.
_____Pain has restricted my social life to my home.
_____I have hardly any social life because of my pain.

Traveling
_____I get no increased pain when traveling.
_____I get some pain while traveling, but none of my usual forms of travel make it any worse.
_____I get increased pain while traveling, but it does not cause me to seek alternative forms of travel.
_____I get increased pain while traveling which causes me to seek alternative forms of travel.
_____My pain restricts all forms of travel except that which is done while I am lying down.
_____My pain restricts all forms of travel.

Employment/Homemaking
_____My normal job/homemaking activities do not cause pain.
_____My normal job/homemaking activities increase my pain, but I can still perform all that is required of me.

_____I can perform most of my job/homemaking duties, but pain prevents me from performing more physically stressful activities (ex. lifting, vacuuming)
_____Pain prevents me from doing anything but light duties.
_____Pain prevents me from doing even light duties.
_____Pain prevents me from performing any job or homemaking chores.

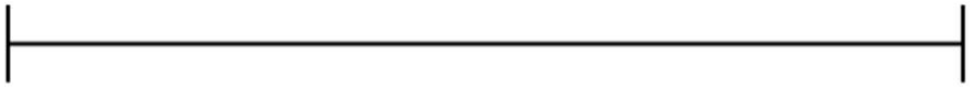
Section 3: To be completed by the researcher:
SCORE: _____%

APPENDIX G

PAIN SEVERITY SCALE

VISUAL ANALOG SCALE (VAS)

How would you rate the pain you felt in your low back? (mark rating using a vertical line)



No pain Worst Imaginable

APPENDIX H

RECRUITMENT ADVERTISEMENT

Participants Needed for Research

Participants are needed for a study to determine the role of genes in Low Back Pain. Participants will be required to give a small amount of blood, fill out a demographic questionnaire, a pain questionnaire a perceived stress and job stress questionnaire.

Requirements:

- Over the age of 18 years
- Currently in or were in jobs involving manual labour
- Suffering from Low back pain
- Females cannot be pregnant

Participants will be compensated $10 for participation. Participation in study will not at any time affect the commitment of your health care providers to administer care or the quality of your care. There will be no loss of benefits to which you are otherwise entitled. Participation will not be revealed to your current employer, to any future employers, nor health insurance providers.

Please call 727-415-4692 or email ng116@msstate.edu if you are interested or need further information.

Primary Researcher: Nirathi Keerthi Govindu, Industrial and Systems Engineering Department, MSU.

IRB Approval Number: 10-282

APPENDIX I

LETTER OF SUPPORT

Starkville
ORTHOPEDIC
CLINIC

W. Todd Smith, M. D.

R. Allen Butler, M. D.

Michael Cox, M. D.

Mary Smith, CFNP

Maggie Fair, CFNP

July 29, 2010

To Whom It May Concern:
This letter is in regard to the recent proposal by Nirabhi Keerthi Govindu. I am writing this letter in support of Keerthi's research proposal and I will be assisting with the recruitment of patients for her research study. If you have any questions, please don't hesitate to contact me.

Sincerely,

R. Allen Butler, M.D.
RAB/am

100 WILBURN WAY • STARKVILLE, MS 39759 • OFFICE 662.320.4008 • FAX 662.323.0029
www.starkvilleortho.com

APPENDIX J

SCORING OF OCCUPATIONAL FACTORS BASED ON RULA SCORING GUIDELINES

POSTURE:

0^o	+1	≥ 8hrs	+4
0^o - 20^o	+2	4 – 8 hrs	+3
20^o - 60^o	+3	2 – 4 hrs	+2
> 60^o	+4	< 2hrs	+1
Side-bending	+1		
Twisting	+1		

Possible Scores: 1 - 10

FORCE:

Less than 4.4lbs of intermittent force/load	+0	≥ 8hrs	+4
4.4 to 22lbs of intermittent force/load	+1	4 – 8 hrs	+3
4.4 to 22lbs of static/repeated force/load	+2	2 – 4 hrs	+2
22lbs or more intermittent force/load	+3	< 2hrs	+1
22lbs or more of static/repeated force/load	+3		

Possible Scores: 0 - 7

REPETITION:

Less than 30 seconds	+3	≥ 8hrs	+4
30 seconds to 1 minute	+2	4 – 8 hrs	+3
Greater than 1 minute	+1	2 – 4 hrs	+2
		< 2hrs	+1

Possible Scores: 1 - 7

VIBRATION:

Job involve activities that subject you to whole body vibration	+1	≥ 8hrs	+4
		4 – 8 hrs	+3
		2 – 4 hrs	+2
		< 2hrs	+1

Possible Scores: 1 - 5

Total Possible Scores: 2 – 29

APPENDIX K

JUSTIFICATIONS FOR COMBINING CATEGORIES

In order to justify combining the categories for physical activity levels, calculations based on MET (Metabolic Equivalent of Task) values were done in order to compare the energy expenditures for each category (Table A).

Table A: Physical activity levels and energy expenditures

Levels	Energy expenditure (kcal/week)	No. of participants	Combined
< 3 times a week (short workouts)	0 to 480	27	No to Low
< 3 times a week (long workouts)	480 to 960	2	
3 to 5 times a week (short workouts)	720 to 1200	13	
3 to 5 times a week (long workouts)	1440 to 2400	11	Moderate to High
>5 times a week (short workouts)	>1440	4	
>5 times a week (long workouts)	>2880	3	

The energy expenditure values are calculated based on MET values where 1 MET = 1kcal/kg/hr. The above are calculated for a person weighing 60 Kg for an activity of running which has a MET value of 8. Short workouts are for 30 minutes and long workouts are for an hour. Based on the energy expenditure values and the number of participants in each category, the categories were combined to form 2 categories of no to low and moderate to high.

In case of alcohol consumption and smoking habits, the levels were combined to 2 overall levels of no and yes. This was based on the participant distribution (see tables B and C) and to test the effect of the presence of any amount of alcohol consumption and smoking on LBP.

Table B: Alcohol consumption

Levels	No. of participants	Combined
Abstain	27	No
3/week	21	Yes
4 to 14/ week	12	
>14/week	0	

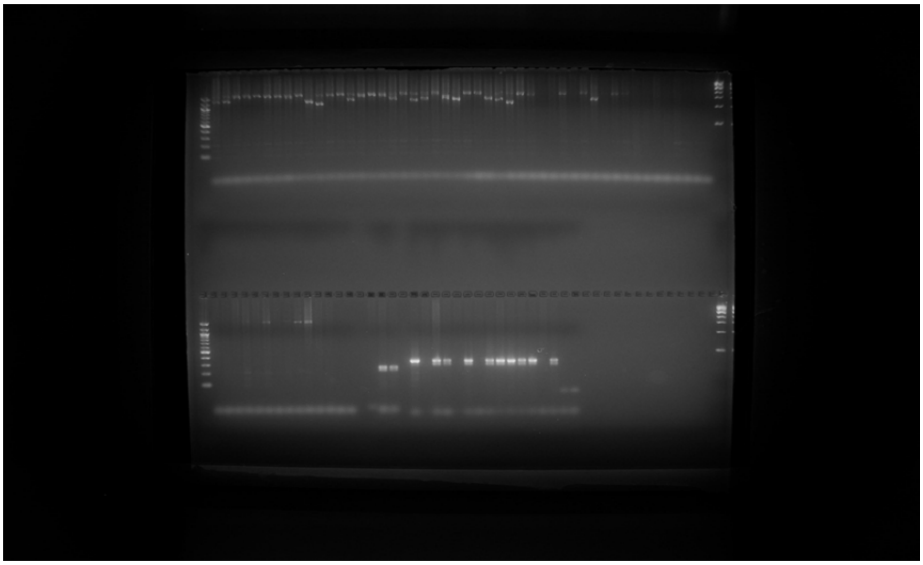
Table C: Smoking habits:

Levels	No. of participants	Combined
None	42	No
< 5 /day	4	Yes
5 to 10/day	9	
10 to 15/day	4	
>15/day	1	

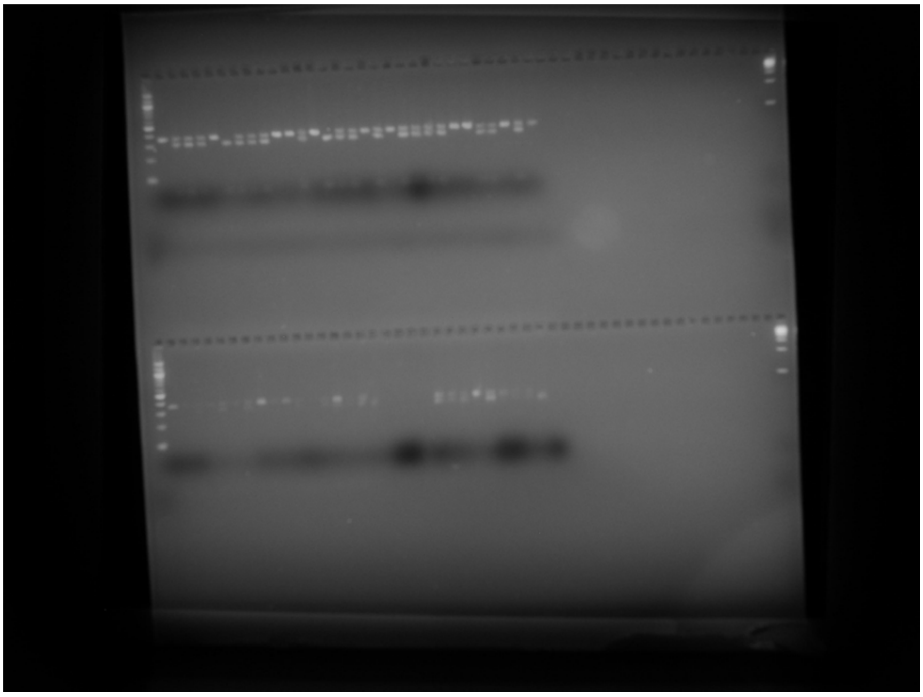
APPENDIX L

AGAROSE GEL ELECTROPHORESIS GEL IMAGES

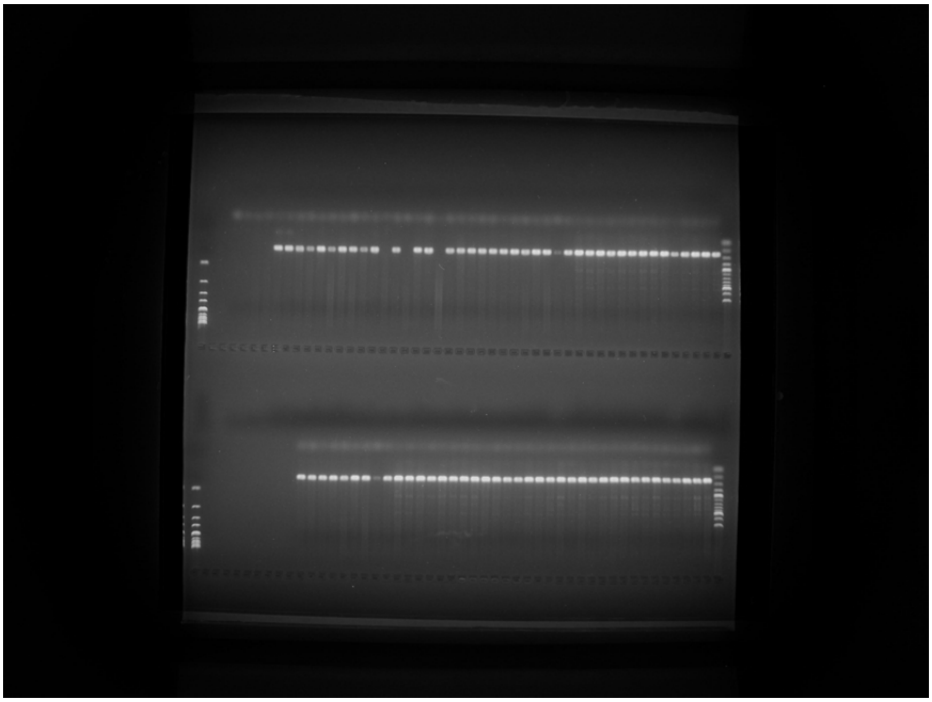
AGC1



VDR (Taq polymorphism)



COL9A3



IL1-RN