THE PROGRESSION FROM ACUTE TO CHRONIC LOW BACK PAIN:

A SYSTEMATIC REVIEW OF RISK FACTORS

AND PRACTICE RECOMMENDATIONS

by

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DEDICATION

To my parents for their unwavering support of my pursuits, ventures, and adventures. Thank you for your good counsel and encouragement no matter how outlandish, overly pragmatic, or out of character the idea springing forth in my mind.

To my husband who sincerely believes I'm capable of whatever I put my mind to and is readily there with emotional and intellectual support. The "thank yous" are endless. In brief, thank you for the delicious meals and for doing ALL the dishes as I've trudged through graduate school.

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ABSTRACT

Acute low back pain (LBP) is common and can lead to chronic LBP. Chronic LBP carries the risk of significant financial burden and reduced quality of life. If low back pain persists beyond six weeks, the likelihood of recovery is limited. Therefore, it would be beneficial to identify those acute LBP patients most at risk of progressing to chronic LBP early in the disease process. This project seeks to identify acute LBP risk factors (RFs) that are most predictive of chronic LBP in primary care populations. A systematic review of literature was undertaken in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines. Article review resulted in the inclusion of 13 studies with 3,641 subjects, evaluating 104 RFs. Data extraction and analysis based on the review protocol resulted in clinical practice and future research recommendations. Coping by catastrophizing and the patient's perspective of risk of chronicity are the most well-supported RFs identified and can be safely assessed in clinical practice for the purpose of recognizing those acute LBP patients most at risk of chronicity and in need of early intervention. An additional 82 RFs are discussed for their value in future research and potential implications for future clinical practice.

CHAPTER ONE

INTRODUCTION AND LITERATURE REVIEW

Nonspecific low back pain (LBP) affects many Americans. It is defined as back pain between the distal margin of the 12th rib and the gluteal folds (Hoy et al., 2014), in the absence of specific pathology, such as vertebral fracture or metastatic cancer. At any given time, 9.4% of the population experiences LBP (Hoy et al., 2014). Over the course of one month, this rises to nearly 25% of the population (Hoy et al., 2012). Acute LBP is pervasive and was traditionally believed to have a good prognosis. Nurse Practitioners (NPs) could expect recovery within six weeks for the majority of acute LBP patients with little to no clinical intervention (Itz, Geurts, van Kleef, & Nelemans, 2013).

However, previous assumptions of rapid recovery for the majority of acute LBP patients may be inaccurate. Current research continues to support the concept of rapid recovery (within 6-12 weeks from onset) in those acute LBP patients who do recover, yet there is disagreement about the prevalence of recovery from acute LBP (Itz et al., 2013; & Menezes Costa et al, 2012). This is in part due to heterogeneity in definitions of recovery and research methods (Menezes Costa et al, 2012). Some research suggests the majority of acute LBP patients progress to recovery (Menezes Costa et al., 2012), while other research suggests that as many as 67% of acute LBP patients progress to chronic LBP (Itz et al., 2013). All seem to agree, however, that, if pain persists beyond 6 to12 weeks, the likelihood of recovery is small (Itz et al., 2013; & Menezes Costa et al., 2012). There is, therefore, a limited opportunity for LBP recovery.

Additionally, we understand chronic LBP to have a profound impact on patient quality of life and healthcare costs in the United States (U.S.) and globally. Based on the Global Burden of Disease 2010 study, LBP is the leading cause of disability in the U.S. and around the world (Hoy et al., 2014; & U.S. Burden of Disease Collaboration, 2013). Furthermore, chronic LBP is associated with significantly increased rates of pain-related comorbidities, polypharmacy, opiate use, and disability. This results in increased expenses. In the U.S., the average annual healthcare costs per chronic LBP patient are estimated to be nearly $5,000 more than those without chronic LBP (Gore, Sadosky, Stacey, Tai, & Leslie, 2012). It follows that direct and indirect LBP care cost estimates range between $119.1 and $238.1 billion annually (inflation-adjusted to 2013) (Ma, Leighton, & Carruthers, 2014).

Given the limited opportunity for recovery and the outcomes of chronicity, LBP care warrants evaluation for evidence-based improvement. This is further supported by the Department of Health and Human Services' (DHHS) 2016 National Pain Strategy, which "aims to decrease the prevalence of pain" (p. 6). Among other clinical goals, the Pain Strategy promotes measures that prevent progression from acute to chronic pain conditions (DHHS, 2016). Therefore, in the interest of supporting NPs in their efforts to prevent the progression from acute to chronic LBP, this systematic review seeks to address the research question: Of studied risk factors (RFs) assessed in the acute phase of LBP (6 weeks or less), which are most predictive of progression to chronic LBP (12 weeks or more)?

Over the course of the last 15 years, several researchers have conducted systematic reviews, evaluating acute LBP RFs predictive of chronic LBP. However, the majority of these reviews focus on a specific RF or set of RFs (such as psychological RFs) in evaluation of their prognostic qualities (Hallergraeff, Krijnen, van der Schans, & de Greef, 2012; Hartvigsen, Kongstad, & Hestbaek, 2015; May & Alessandro, 2012; Pincus, Burton, Vogel, & Field, 2002; Pinheiro et al, 2016; Ramond et al, 2011; Wertli et al, 2014a; & Wertli, Rasmussen-Barr, Weiser, Bachmann, & Brunner, 2014b). While this approach is of value, it does not result in a comprehensive set of clinically relevant predictive RFs.

Some reviews incorporate findings from studies that include subacute (Hallegraeff et al., 2012; Hartvigsen et al., 2015; Pincus et al., 2002; Pinheiro et al., 2016; Ramond et al., 2011; & Wertli et al., 2014a) and chronic (Hartvigsen et al., 2015) LBP sufferers, without group delineation. This technique provides a broad picture of LBP sufferers, but does not produce results that are specific to the acute LBP patient at risk of chronicity. Subacute and chronic LBP sufferers are already at increased risk of continued pain due to symptom duration beyond six weeks (Itz et al., 2013; & Menezes Costa et al., 2012). Therefore, in these cases, the outcome of interest is arguably already present at time of initial assessment. Some of these reviews also include studies from Workers Compensation (WC) populations in addition to primary-care populations (Hallergraeff et al., 2012; Hartvigsen et al., 2015; Pincus et al., 2002; Pinheiro et al., 2016; Ramond et al., 2011; Wertli et al., 2014a; & Wertli et al., 2014b). Given the potential secondary gains

of prolonged LBP in WC populations, WC studies may introduce bias within review findings, limiting the generalizability of results to the primary-care setting.

Two previous reviews take a broader look at LBP RFs (Chou & Shekelle, 2010; & Melloh et al., 2009). However, both included WC studies (Chou et al., 2010; & Melloh et al., 2009) and one included groups with sub-acute and chronic LBP sufferers (Melloh et al., 2009). This methodology limits generalizability to the acute LBP patient presenting to the primary-care setting. Both reviews excluded RFs that did not fit into the review's established framework (Chou et al., 2010; & Melloh et al., 2009) and one excluded studies from which Likelihood Ratios could not be calculated (Chou et al., 2010). These processes potentially eliminated relevant studies and risk factors from review. Therefore, this project is, to our knowledge, the first comprehensive review of acute LBP RFs that are predictive of chronic LBP in the primary-care setting.

CHAPTER TWO

THEORETICAL UNDERPINNINGS

The Modeling and Role-Modeling (MRM) nursing theory provided theoretical guidance throughout this project. MRM is a grand nursing theory in which patient care is conducted within the context of "modeling" and "role-modeling." "Modeling" is a process by which the NP gains "an understanding of the client's world from the client's perspective" (Hertz, 1997, p.1). Once the NP gains this in-depth understanding of the patient's world, "role-modeling" guides collaborative-care planning to meet the patient's needs. Throughout the process of MRM, the NP will consider biophysical, psychological, social, cognitive, spiritual drive, and genetic base as they relate to the patient's experience (Erickson, Tomlin, & Swain, 1983, p. 45). The process of MRM is conducted with unconditional acceptance of the patient and the end goal of holistic health (Hertz, 1997).

This project was, therefore, conducted from a holistic perspective, considering that biophysical, psychological, social, cognitive, spiritual, and genetic factors likely play a role in the patient's experience of LBP. Every previously studied RF was thus considered and evaluated. Furthermore, the project was undertaken with a broad model of the chronic LBP sufferer's world, based on clinical experience and our current evidence-based understanding of acute and chronic LBP. In this manner, the review protocol was developed to pragmatically evaluate a body of evidence regarding RFs

while allowing for consideration of how the results may impact the individual NP's understanding of the individual LBP sufferer's world.

CHAPTER THREE

METHODS

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Liberati et al., 2009). Meta-analysis was not attempted due to the heterogeneity of results, research methods, and definitions of outcomes among studies per the PRISMA guidelines (Liberati et al., 2009). The systematic review protocol was developed, under consultation with Statistical Consulting Research Services, prior to start of the review process and modified where appropriate during the process, as described briefly throughout this section. For a comprehensive description of the review protocol and points of modification, refer to Appendix A.

Databases, including CINAHL, Web of Science, and Psych Info were searched with the following search terms and Boolean operators: "low back pain" AND (acute or subacute or "sub acute" or "sub-acute") AND (predic* or prognostic). Searches included no limits on date of publication or article type and the final search was conducted on October 16, 2016. After excluding duplicate articles, one non-blinded reviewer (WS) evaluated all titles and abstracts. If an article appeared to meet inclusion/exclusion criteria described in Figure 1, based on title and abstract review, the full text was retrieved and reviewed. Full-text articles meeting inclusion/exclusion criteria were retained for further analysis.

INCLUSION CRITERIA:

- All subjects were between the ages of 18 and 65 years old.
- Subjects' LBP had been present for 6 weeks or less, or study results are stratified based on duration of symptoms with results specific to those who had pain for 6 weeks or less.
- Outcome measures were assessed at least 12 weeks after pain onset.
- Outcome assessment included a measure of pain or disability.

EXCLUSION CRITERIA:

- All subjects had work related LBP or a WC LBP claim.
- Subjects were part of a randomized trial and/or had received an intervention beyond usual care as defined by the individual study.
- Risk factors studied are not easily assessed in primary care setting.
- Written in a language other than English.

LBP- Low back pain, WC- Workers Compensation

Figure 1: Criteria to determine study inclusion in or exclusion from systematic review.

Data was then extracted from all retained studies and organized by RF within evidence tables. Recorded measures included study design, sample size, RFs and assessment methods, outcome measures and assessment methods, outcome time points, methods of statistical analysis, and results. All studied RFs were included for further analysis to allow for a comprehensive review.

Once measures of interest were extracted from included studies, each study was evaluated for risk of bias using the Newcastle-Ottawa Scale (NOS) (Wells et al., 2014) as recommended by the Cochrane Handbook (The Cochrane Collaboration, 2011). The NOS is designed specifically for nonrandomized studies and evaluates the cohort selection, comparability, and outcome, resulting in a score of 0-9. Scores of 0-3 were considered to represent poor quality, 4-6 acceptable quality, and 7-9 good quality (Schroder, Boisen, Reimers, Teilmann, & Brok, 2016). In addition to the NOS scoring, the most frequently studied RFs were identified. Each study was then assigned a Study Quality (SQ) score based on its NOS score, sample size, and the percent of top-studied

risk factors included in the analysis. The SQ score then acted as a measure of quality with which study results could be compared.

RFs in which all studies unanimously agreed to lack of predictive value were removed from further evaluation. In RFs where studies showed disagreement in predictive value, the sum of SQ scores from studies showing predictive value was compared to the sum of SQ scores from studies showing lack of predictive value. Where the sum of SQ scores showing predictive value was greater than that showing lack of predictive value, the RF was retained for further analysis. All other RFs were excluded from further analysis. The remaining RFs were then ranked with an RF score based on agreement among studies, percent of review studies in which it was evaluated, and NOS scores.

A post hoc analysis was also completed on all excluded risk factors with the purpose of identifying those that may warrant further research, despite current evidence demonstrating no predictive value. The post hoc analysis was conducted in a similar fashion to the primary analysis, taking into consideration the same measures of quality and resulting in a Modified Risk Factor (MRF) score. However, contrary to scoring in the primary analysis, RFs evaluated in the post hoc analysis with low NOS scores or that were less frequently studied among review studies were given higher MRF scores for the purpose of identifying those RFs requiring further, higher quality evaluation of predictive value. See Figure 2 for a visual summary of the review protocol.

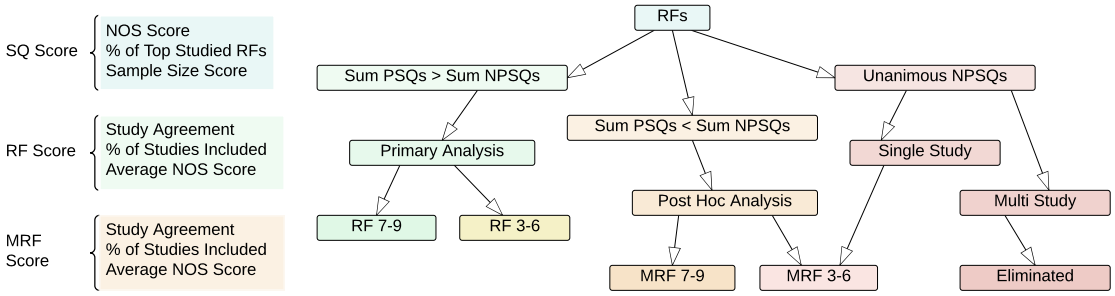

Figure 2: Review protocol summary
SQ- Study Quality, NOS- Newcastle Ottawa Scale, RF- Risk Factor, MRF- Modified Risk Factor, PSQs- Predictive Study Quality Scores, NPSQs- Non-Predictive Study Quality Scores,.

Figure 2: Visual summary of systematic review protocol for individual study analysis and RF analysis.

CHAPTER FOUR

RESULTS

The search strategy retrieved 676 references. Title, abstract, and full-text review resulted in inclusion of 13 observational cohort studies (Bakker, Verhagen, Lucas, Koning, & Koes, 2007; Burton, Tillotson, Main, & Hollis, 1995; Coste, Delecoeuillerie, Cohen de Lara, Le Parc, & Paolaggi, 1994; Dixon & Gatchel, 1999; Gatchel, Polatin, & Mayer, 1995; Grotle et al, 2005; Grotle, Brox, Glomsrød, Lønn, & Vøllestad, 2007; Henschke et al., 2008; Mehling, Ebell, Avins, & Hecht, 2015; Melloh et al., 2013; Schiottz-Christensen et al., 1999; Sieben et al., 2005; & Swinkels-Meesisse et al., 2006), as described in Figure 3.

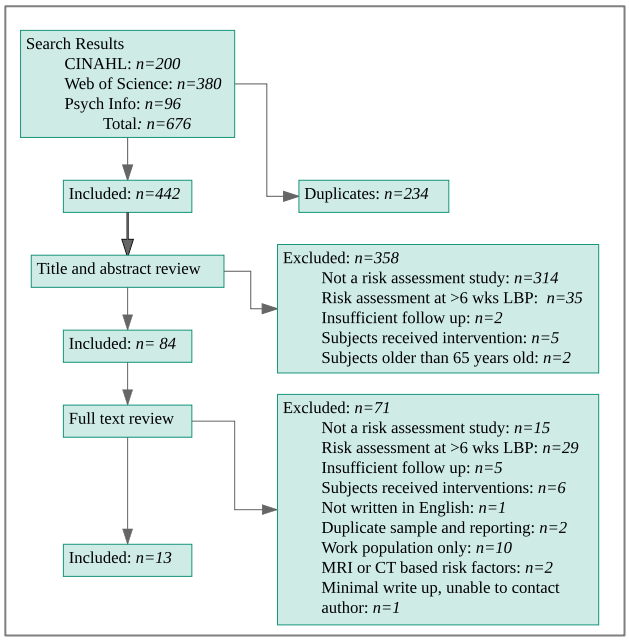

Figure 3: Summary of study title, abstract, and full text review resulting in exclusion and inclusion of studies for further analysis.

Primary Author & Yr.	Sample Size	NOS Score	Outcome Measures	Outcome Assessment	Factors Identified by Study as Significant	Analysis
Bakker, 2007	n=88	6	Subject report of recurrence or pain lasting over 12 wks.	6 mos.	Age & Smoking	Regression analysis
Burton, 1995	n=186	6	RMDQ score	1 yr.	CSQ-Catastrophizing, Modified somatic perceptions questionnaire, Straight leg rise test, CSQ-Praying/Hoping, Leg pain	Regression analysis
Coste, 1994	n=92	7	Pain score, ability to stand, & RMDQ	8, 15, 30, 60, & 90 days	Unemployment, Previous episode of chronic LBP, Worsened pain with standing, Worsened pain with lying, RMDQ score, Compensation	Regression analysis
Dixon, 1999*	n=435	5	Structured telephone interview regarding return to work	12 mos.	Female gender, Single marital status, Number of children, Single parent, WC	Comparative analysis
Gatchel, 1995*	n=421	5	Structured telephone interview regarding return to work.	6 & 12 mos.	Million visual analog scale score (disability), WC, Female gender, MMPI Scale 3 (hysteria)	Regression analysis
Grotle, 2005**	n=123	9	Average pain over last week & RMDQ score of $\leq$ 4.	3 mos.	>45 yrs. of age, Smoking, Positive neurological signs, ALBSQ, HSCL (distress)	Regression analysis
Grotle, 2007**	n=112	9	Average pain over the last wk. and RMDQ score of $\leq$ 4.	1, 3, 6, 9, & 12 mos.	ALBSQ, HSCL (distress)	Regression analysis
Henschke, 2008	n=969	8	Subject rating of pain intensity, study specific rating of disability, & return to work.	6, 12 wks., & 1 yr.	Age, Pain intensity, Study specific rating of depression, Subject's perceived risk of chronicity, Compensation, Reduced activity, Duration	Regression analysis
Mehling, 2015	n=510	7	Subject rating of perceived recovery & pain intensity.	6 mos. & 2 yrs.	Pain in upper back, Pain below the knee, Subject perceived risk of chronicity, CSQ-Catastrophizing, CSQ-Ignoring Pain	Regression analysis
Melloh, 2013	n=151	7	Oswestry Disability Index score	3, 6, 12 wks. & 6 mos.	PCS-Magnification & rumination subscales, Modified Zung Depression Inventory	Analysis of covariance
Schiottz-Christensen, 1999	n=503	8	Study specific questionnaire on functional recovery & sick leave.	1, 6, & 12 mos.	> 40 yrs. of age, Male gender, Previous sick leave from LBP, Disabled, Practitioner belief: Subject LBP is caused by work, Subject is likely to develop chronic LBP, & subject is vulnerable to stress	Regression analysis
Sieben, 2005	n=167	6	GCPS	3, 6, & 12 mos.	Age by study specific category, Number of previous episodes, Low education, Pain intensity	Regression analysis
Swinkels-Meewisse, 2006	n=431	6	RMDQ & participation items from GCPS.	6 wks. & 6 mos.	Age, Lack of sports, Duration, Radiation, Prior episode, Pain intensity, TSK- selected items (fear avoidance beliefs), Education, Participation	Random intercept models

* Duplicate sample. Variation in sample size is due to variation in reporting style.
** Duplicate sample. Variation in sample size is due to variation in loss to follow up at different time points.
RMDQ-Roland Morris Disability Questionnaire, CSQ- Coping Strategies Questionnaire, LBP- Low Back Pain, WC- Worker's Compensation, MMPI- Minnesota Multiphasic Personality Inventory, ALBSQ- Acute Low Back Screening Questionnaire, HSCL-Hopkin's Symptom Check List, PCS- Pain Catastrophizing Scale, GCPS- Graded Chronic Pain Scale, TSK-Tampa Scale of Kinesiophobia

Table 1: Summary of studies included in systematic review.

This group of studies evaluated 10 distinct samples of acute LBP sufferers, with an across-study total of 3,641 subjects. Overall, included studies evaluated 104 RFs for predictive value in progression from acute to chronic LBP. Six RFs were identified as being evaluated in the majority of studies. These included age, gender, duration of current symptoms, radiation to leg, depression, and disability. All studies were considered as acceptable to strong quality, based on NOS scores (Wells et al., 2014; & Schroder et al, 2016). See Table 1 for a summary of individual study characteristics.

Of the 104 evaluated RFs, 70 RFs were eliminated from further review in the primary analysis due to unanimous study agreement of lack of predictive value. The remaining 34 RFs were further evaluated by comparing SQ scores in support of predictive value to those in support of lack of predictive value. Twenty of the remaining RFs were found to have more evidence in support of a lack of predictive value and were, therefore, eliminated from further review in the primary analysis.

Ultimately, 14 RFs were found to show predictive value. Two of these RFs were assigned high RF scores of 7-9, as can be seen in Table 2. The remaining 12 RFs

Risk Factor (Risk Factor Score)	Primary Author & Publication Date	Method of Analysis
Coping by catastrophizing (7)	Burton,1995	CSQ-Catastrophizing subscale
	Mehling,2015	
Subject expectation of chronicity (7)	Henschke, 2008	Subject rating of risk of chronicity on 0-10 scale.
	Mehling, 2015	

CSQ- Coping Strategies Questionnaire.

Table 2: Risk factors with RF scores of 7-9

had RF scores of 3-6 and can be seen in Table 3. Of note, two RFs in Table 3 were found to be protective against chronic LBP, rather than predictive of chronicity. These RFs are denoted by an asterisk.

Risk Factor (Risk Factor Score)	Primary Author & Publication Date	Method of Analysis
Pain intensity now (4)	Bakker, 2007	0-10 VAS
	Burton, 1995	6 point verbal descriptor
	Sieben, 2005	0-100 VAS
	Swinkels-Meewisse, 2006	0-10 VAS
ALBSQ (5)	Bakker, 2007	ALBSQ score
	Grotle, 2005	
Catastrophizing by rumination (5)	Mehling, 2015	PCS, Rumination subscale
	Melloh, 2013	
Coping by ignoring pain (5)	Burton, 1995	CSQ, Ignoring Pain subscale
	Mehling, 2015	
Coping with increased activity* (5)	Burton, 1995	CSQ, Increased Activity subscale
	Mehling, 2015	
Pain intensity on average (6)	Henschke, 2008	Pain over episode
	Mehling, 2015	Pain over last week
Ability to sleep at night* (4)	Mehling, 2015	Subject report of being able to sleep at night
Children (6)	Dixon, 1999	Subject report of number of children
Distress (7)	Grotle, 2005	High score on HSC
Pain worsened with standing (6)	Coste, 1994	Subject report of worsened pain with standing
Previous episode of chronic LBP (6)	Coste, 1994	Subject report of LBP episode lasting >3 mos.
Single parent (6)	Dixon, 1999	Subject report of being a single parent

**Factor is protective against chronic LBP.*
VAS- Visual Analogue Scale, ALBSQ-Acute Low Back Pain Screening Questionnaire, PCS- Pain Catastrophizing Scale, CSQ- Coping Strategies Questionnaire, HSC- Hopkins Symptom Checklist, LBP-Low Back Pain

Table 3: Risk factors with RF scores of 3-6 or 7-9 with only single study evaluation.

Finally, a post hoc analysis was undertaken to evaluate the 20 RFs that were found in the primary analysis to have more evidence supporting lack of predictive value than evidence supporting predictive value. Of these 20 RFs, 12 were found to have MRF scores of 7-9 as seen in Table 4. The remaining eight RFs had MRF scores of 3-6 and are listed in the first column of Figure 4. Additionally, any RF that showed unanimous lack of predictive value, but that was only evaluated in one study, is also included in Figure 4. The remaining twenty RFs with unanimous agreement of lack of predictive value among multiple studies can be found in Figure 5.

Risk Factor (MRF scores)	Primary Author & Publication Date	Method of Analysis
Depression (7)	Burton, 1995	MZDI
	Coste, 1994	DSM III
	Gatchel, 1995	DSM III & MMPI Scale
	Henschke, 2008	Study specific scale
	Mehling, 2015	HKF-R10 (selected items)
	Melloh, 2013	MZDI
	Sieben, 2005	Beck Depression Inventory
Compensation (7)	Coste, 1994	WC
	Gatchel, 1995	WC or personal injury ins.
	Grotle, 2005	Financial compensation
	Henschke, 2008	WC or motor vehicle ins.
LBP effect on usual activity (7)	Henschke, 2008	Days of reduced activity due to LBP
	Mehling, 2015	
	Sieben, 2005	PARS
	Swinkles-Meewisse, 2006	CPGQ-Participation items
Smoking (8)	Bakker, 2007	Subject report of smoking status
	Gortle, 2005	
	Henschke, 2008	
	Mehling, 2015	
Catastrophizing- Magnification (8)	Mehling, 2015	Pain Catastrophizing Scale-Magnification subscale
	Melloh, 2013	
	Sieben, 2005	
Somatization (8)	Burton, 1995	Modified Somatic Perception Questionnaire
	Grotle, 2005	
	Sieben, 2005	TSK-Somatic subsection
Positive straight leg raise test (7)	Burton, 1995	Care provider's physical assessment finding
	Coste, 1994	
	Schiotzz-Christensen, 1999	
Coping by praying and hoping (8)	Burton, 1995	CSQ-Praying and Hoping subscale
	Mehling, 2015	
Neurologic signs (7)	Gortle, 2005	2 or more positive out of 7 physical findings
	Schiotzz-Christensen, 1999	Missing reflexes and muscular paresis
Other areas of pain (8)	Henschke, 2008	Upper back pain
	Mehling, 2015	Neck, shoulder, or upper back pain
Participation in exercise (8)	Henschke, 2008	Regular exercise
	Swinkels-Meeswisse, 2006	Sports activities
Previous LBP episodes (8)	Buton, 1995	Subject report of number of previous episodes
	Sieben, 2005	

MRF- Modified Risk Factor, MZDI-Modified Zung Depression Inventory, DSM III- Diagnostic and Statistical Manual of Mental Disorders, MMPI- Minnesota Multiphasic Personality Inventory, HKF-R10- Heidelberger Kurz-Fragebogen, WC- Worker's Compensation, LBP- Low Back Pain, PARS- Physical Activity Rating Scale, CPGQ-Chronic Pain Grades Questionnaire, TSK-Tampa Scale of Kinesiophobia, CSQ- Coping Strategies Questionnaire

Table 4: RFs with MRF scores of 7-9 in the post-hoc analysis

MRFS 3-6, (number of studies evaluating factor)	**Single study risk factors showing lack of predictive value**			
* Age (10) * Gender (10) * Duration (9) * Pain radiating to leg (8) * Disability (7) * Education (6) * Previous episode, Y/N (6) * FAB-physical activities (5)	* AB physical activity * AB lying down * AB moving back * Alleviated by massage * Bed rest * Body mass index * Catch * Clinician type * CPB develop chronic LBP * CPB vulnerable to stress * CPB of work cause * CPCI-Ask for assistance	* CPCI-Seek social support * Change to job * DRAM (LBP tool) * Ethnicity * Hypochondriasis * Hysteria * Inability to stand * Income * Mechanical load * Muscle pain * Negative Affect * Overt pain behavior * Pain at night * Pain level at worst	* Pain level at onset * PCS-Helplessness * Percussion test * PLOC-Pain responsibility * Prev. LBP consult * Prev. LBP hospitalization * Prev. lumbar x-ray * Prev. manual therapy * Prev. chiropractic therapy * Prev. LBP sick leave * Prev. LBP surgery * Prev. LBP physical therapy	* Red flags * Restricted spine PROM * Root tension * Sit up test * Sleep/relax medication * Stop act. if pain worsens * Stress * Subject RTW thoughts * Substance abuse * Tolerable pain level * Transfer of pain * Trunk list

FAB- Fear avoidance beliefs, AB- Aggravated by, CPB- Care provider belief, CPCI- Chronic Pain Coping Inventory, DRAM- Distress and Risk Assessment Method, PCS- Pain Catastrophizing Scale, PLOC-Pain Locus of Control Assessment, Prev.- Previous, PROM- Passive Range of Motion

Figure 4: RFs with MRF scores of 3-6 and single study RFs showing lack of predictive value.

Risk Factors Lacking Predictive Value (number of studies evaluating factor)		
AB Impulsion (2)	FAB regarding work (3)	Pain level at best (2)
Ability to decrease pain (3)	General health tools (2)	Pain medication use (2)
Anxiety (4)	Job satisfaction (4)	Sick leave with current LBP (3)
CSQ-Divert attention (2)	Marital status (4)	Spine active range of motion (4)
CSQ-Pain sensation (2)	Minority (3)	Sudden onset of symptoms (5)
CSQ-Self statements (2)	McGill Pain Questionnaire (2)	Work type (2)
Employment status (5)	Native to country of study (2)	

AB-Aggravated by, CSQ- Coping Strategies Questionnaire, FAB-Fear avoidance beliefs

Figure 5: Risk factors lacking predictive value

CHAPTER FIVE

DISCUSSION AND RECOMMENDATIONS

Of the 14 RFs evaluated in the primary analysis, coping by catastrophizing and subject expectation of chronicity have the strongest evidence in support of use in clinical practice. Clinical assessment of these RFs carries little to no risk for the patient, would help the NP identify those acute LBP patients most at risk of progressing to chronic LBP, and adjust the treatment plan accordingly. Furthermore, evaluating these two RFs would help the NP to develop a clearer understanding of the LBP patient's world from their perspective. Therefore, these two risk factors will be discussed in further detail.

Coping by catastrophizing was assessed using the Coping Strategies Questionnaire (CSQ) catastrophizing subscale (Burton et al., 1995; & Mehling et al., 2015). The CSQ is a written questionnaire developed in 1982 to evaluate the coping strategies of chronic LBP patients (Rosentiel & Keefe, 1983). It takes 5 minutes to complete and includes eight subscales assessing cognitive and behavioral coping mechanisms with a 0-6-point Likert scale where 0 means never when in pain and 6 means always when in pain (Abbott, 2010). Since its development, the CSQ has been used by several researchers, and the full questionnaire and its subscales consistently show good internal consistency and test-retest reliability (Abbott, 2010).

There is discrepancy among the review studies in how the CSQ catastrophizing subscale was used. One study used a single item from the six-item catastrophizing subscale (Mehling et al., 2015), while the other assessed subjects with the full CSQ and

evaluated results from each subscale (Burton et al., 1995). Both techniques rendered significant results and one approach cannot be recommended over the other for clinical application. Figure 6 lists all six questions from the CSQ catastrophizing subscale (Rosentiel et al., 1983) with an asterisk denoting the single question used in both studies.

CSQ CATASTROPHIZING SUBSCALE:

- It's terrible and I feel it's never going to get better *
- It's awful and I feel it overwhelms me
- I feel my life isn't worth living
- I worry all the time about whether it will end
- I feel I can't stand it anymore
- I feel like I can't go on

**Question used in both review studies*

Figure 6: CSQ catastrophizing subscale questions

Subject expectation of chronicity was assessed using the same question across relevant review studies: "In your view, how large is the risk that your pain may become persistent?" (Henschke et al., 2008; & Mehling et al., 2015). Subjects were asked to rate their risk from 0-10 where 0 is no risk and 10 is high risk (Henschke et al., 2008; & Mehling et al, 2015). Both studies found significant risk of progression to chronic LBP with high subject-risk ratings.

While a specific clinical assessment tool or method cannot be developed or recommended based on these findings alone, they do help to inform the practice of an NP caring for the acute LBP patient. Simply asking a patient to rate their risk of persistence and a question or questions from the CSQ catastrophizing subscale (Figure 6) will provide the NP with important information that may impact the course of the LBP patient's collaborative-care plan over the first six weeks in which the patient has the best

chance of recovery. That being said, further research is needed before a robust and well-supported clinical risk assessment tool can be developed.

Future research efforts should include further assessment of both the RFs discussed thus far and those found in Table 3. The RFs found in Table 3 represent those in which the bulk of the evidence was in support of predictive value, but also included some evidence demonstrating lack of predictive value or unanimous support of predictive value, but lower quality evidence. Therefore, further research is needed before clinical practice recommendations can be made regarding this group of RFs. Nonetheless, some or all of Table 3's RFs will likely play an important predictive role in future acute LBP care.

Additionally, those RFs found in Table 4 may also play a role in future research. These are the RFs excluded from the primary analysis but identified in the post hoc analysis as having some support of predictive value. Albeit less likely, those RFs found in Figure 4 may also play a role in future research. These are the RFs with very little evidence in support of predictive value, lower quality evidence, or showing lack of predictive value in a single study. Further research is therefore needed before we can definitively conclude potential clinical application or lack thereof for the RFs evaluated in the post hoc analysis (Table 4 and Figure 4). However, those RFs unanimously identified in multiple studies as showing lack of predictive value (Figure 5) may be excluded from future research.

Despite these findings, two RFs with little to no evidence of predictive value warrant further discussion: age and pain-medication use. Most of the studies assessing

age as an RF, analyzed it as a continuous variable as part of a regression analysis (Bakker et al., 2007; Burton et al., 1995; Coste et al., 1994; Henschke et al., 2008; Mehling et al., 2015; & Swinkels-Meewisse et al., 2006). This method analyzes the increased risk of developing chronic LBP for each one year of age, generally showing a lack of significance. It stands to reason that an assessment of age based on age categories may show more consistently significant results. In one of the review studies, age was evaluated as an RF for subjects over 45 years old, with significant findings (Grotle et al., 2005). Therefore, age may play a more important predictive role than demonstrated in this review and should be included in future research as a categorical rather than continuous variable.

Pain-medication use was found in this review to have no predictive value or need for future research. It should be noted, however, that there was no delineation between opiate and non-opiate pain-medication use in the relevant review studies (Grotle et al., 2007; & Henschke et al., 2008). Given the mounting evidence regarding the risks of early opiate use in WC populations (Carnide et al., 2017), it stands to reason that a more focused assessment of opiate-medication use in acute LBP primary-care patients may provide more significant findings. Therefore, further research is indicated despite the findings of this review.

Finally, future research should make efforts toward consistency of methods of assessment and definitions of recovery. One of the main limitations of this review is the heterogeneity of techniques and definitions used in included studies. This is clearly seen in Table 1 when comparing the outcome measures and tools for included review studies.

Even studies using the same tool often had different cutoff values for recovery. It is beyond the scope of this review to make specific suggestions on the most appropriate outcome measure for future research. However, it would be prudent for future researchers to utilize an already established outcome measure used in one of the included review studies.

In addition, this review carries with it the risk of publication bias. Search strategies did not limit article type in an effort to include varied sources of data, but it is likely that there are unpublished studies with lack of significant findings regarding this topic. The relatively small sample sizes of some included studies are also a limitation of this review. However, excluding studies with small sample sizes would have resulted in a less comprehensive review. Additionally, the article review, data extraction, and RF analyses were completed by a single, non-blinded reviewer (WS), which introduces the potential for personal bias. Every attempt was made to mitigate this risk, namely by creating a rule-based review protocol and by strictly adhering to the established rules, making notes of any exceptions with supporting rationale.

This is, to our knowledge, the first comprehensive review of acute LBP RFs predictive of progression to chronic LBP in primary-care populations. No limitations were made on RF inclusion. Based on these review findings, assessments of patient coping by catastrophizing and patient expectation of progression to chronicity can safely be incorporated into the NP's acute LBP patient assessment as an aid in identifying those patients who are at risk of developing chronic LBP. Several RFs were identified as important for continued research efforts toward improved clinical assessment of the acute

LBP patient (Tables 2, 3, 4, and Figure 4) while others were identified as not having research value (Figure 5). There is much work to be done before we have a clear and comprehensive understanding of acute LBP RFs predictive of chronic LBP. However, the research findings to this point, as summarized in this review, will act as a solid foundation for future research efforts.

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APPENDIX A

REVIEW PROTOCOL

The following outline is a comprehensive description of the final low-back-pain (LBP) study protocol. Areas of modification from original study protocol are marked with an asterisk followed by a description of the original protocol measure where indicated and rationale for modification.

1. Research Question: Of studied risk factors (RFs) assessed in the acute phase of LBP (six weeks or less), which are most predictive of progression to chronic LBP (12 weeks or more)?

2. Search Strategy: Developed under the guidance of a reference librarian (personal communication, Mary Anne Hansen, May, 2015).
    a. Databases to be searched: CINAHL, Web of Science, and Psych Info
    b. Search terms and Boolean operators: “low back pain” AND (acute or subacute or “sub acute” or “sub-acute”) AND (predic* or prognostic).

3. Study Review Process
    a. All retrieved references and abstracts will be imported into and sorted in End Note X7 (Thomas Reuters [Scientific] LLC, Philadelphia, PA, USA).
    b. Duplicate references will be removed.
    c. All titles and abstracts will be reviewed by a single, non-blinded reviewer (WS) to evaluate conformity with inclusion and exclusion criteria. Studies will be eliminated from further review if inclusion criteria are not met or exclusion criteria are present based on title and abstract review.
        i. Inclusion Criteria:

1. Subjects were between the ages of 18 and 65 years old.
2. Subjects' LBP had been present for six weeks or less at time of initial assessment, or results are stratified based on subjects' duration of symptoms with results specific to those who have had pain for six weeks or less.*
3. Outcome measures were assessed at least 12 weeks after pain onset.
4. Outcome assessment included a measure of pain or disability.

ii. Exclusion Criteria:

1. All subjects had work-related LBP or a Worker's Compensation LBP claim.**
2. Subjects were part of a randomized trial and/or had received an intervention beyond usual care as defined by the individual study.
3. RFs studied are not easily assessed in the primary-care setting.
4. Written in a language other than English.

d. Full-text articles will be retrieved for all other titles and abstracts for further review. Those full-text articles meeting inclusion criteria and without exclusion criteria will be retained for systematic review of evidence.

**Original inclusion criteria #2 did not allow for stratified results. However, one study was identified in which acute, subacute, and chronic LBP patients were studied and results stratified based on symptom duration at initial assessment. By including studies with stratified results, we allowed for inclusion of additional, appropriate studies without introducing risk of bias.*

***Initially, studies focusing strictly on WC and work-related LBP were to be included. However, it became apparent that this population of LBP sufferers is different than the primary-care population. This difference is most apparent in primary care-studies that identify compensation of any form to be a risk for chronicity (Coste, Delecoeuillerie, Cohen de Lara, Le Parc, & Paolaggi, 1994; Gatchel, Polatin, & Mayer, 1995; & Henschke et al., 2008). This suggests that a WC group is inherently at greater risk of progressing to chronicity and would not be a representative sample of a primary-care population which contains both subjects who are and who are not receiving compensation.*

4. Data Extraction Process

    a. Each author list will be compared to author lists from all included studies to aid in identification of duplicate samples. If studies contain one or more of the same authors, sample descriptions will be compared. If duplicate samples are identified, data on each RF evaluated will be extracted from one study only.*

    b. Each RF evaluated in the included studies will have a separate evidence table. Where possible, RFs labeled differently across studies but determined to be assessing the same risk will be combined within the same evidence table.

        i. Each evidence table will include data categories for authors and year published, sample size, study design, RF, method of risk assessment, outcome measure, method of outcome assessment,

time points of outcomes measured, statistical analysis, results pertaining to specific RF, and overall study results.

ii. Where there are multiple time points in which data were collected and analyzed, the first time point representing chronicity (12 weeks or more of LBP) and with complete statistical analysis will be used.

iii. If there is more than one assessment of the same RF within one study, the most significant results will be used.

c. A single, non-blinded reviewer (WS) will extract data of interest from each study, for each RF, and record it in the appropriate evidence table. This will result in data from multiple studies within each RF evidence table. In this manner, all RFs evaluated in included studies will be considered as part of the systematic review.

**Initially, this was not part of the data extraction process. However, a duplicate sample was identified by chance. This measure was immediately put in place to prevent double reporting on a single sample.*

5. Primary Analysis* (Developed under the guidance of Jordan Schupbach with Statistical Consulting Research Services [SCRS])

    a. For studies that include odds ratios or hazard ratios with confidence intervals (CI), only results in which the CI does not encompass 1 will be considered as significant (Jewell, 2004).

    b. All RFs in which researchers unanimously agree that there is no predictive value will be eliminated from further review in the primary analysis.

c. Each study will be scored using the Newcastle-Ottawa Scale (NOS) for cohort studies (Wells et al, 2014a). The Newcastle-Ottawa Quality Assessment Scale worksheet (Wells et al, 2014b) will be used as a scoring guide for each study, resulting in a score of 0-9. Scores of 0-3 will be considered of poor quality, 4-6 of acceptable quality, and 7-9 of good quality (Schroder, Boisen, Reimers, Teilmann, & Brok, 2016).

    i. Scoring Details: As established by the NOS (Wells et al., 2014a) unless otherwise noted as a study-specific modification.

        1. Selection

            a. Representativeness of the exposed cohort: One point will be allotted if the cohort was selected from patients seeking care for acute LBP at a primary-care or other clinic setting over a specified period of time and the exposure to the risk factors of interest was evaluated after the subject was entered into the study.

            b. Selection of non-exposed cohort: One point will be allotted if the above parameter is met.

            c. Ascertainment of exposure: One point will be allotted if exposure to the RF of interest is demonstrated in one of three ways: based on secure medical records, based on subject response to a

structured interview, or based on subject response to an established, valid, and reliable written assessment tool, such as the Beck Depression Inventory (the third is a modification to original NOS specific to this study).

1. Given that each risk factor is assessed differently within the same study, this may make for variation of NOS scores by 1 point for the same study.

d. Demonstration that outcome of interest was not present at start of the study: One point will be allotted if the researcher excluded subjects with LBP lasting more than six weeks and designated a period of time prior to the start of current LBP episode in which subjects were free of LBP.

2. Comparability

a. Comparability of cohorts on the basis of design or analysis: One point will be allotted if the study design controls for those patients who have symptoms of specific pathology such as malignancy or vertebral fracture. Another point will be allotted

if the statistical analysis controls for other key factors such as age.

3. Outcome
    a. Assessment of outcome: One point will be allotted if assessment was conducted with blinded subjects and assessors.
    b. Follow up time: One point will be allotted if outcome assessment is completed at least 12 weeks following initial onset of LBP.
    c. Adequacy of follow-up cohorts: One point will be allotted if less than 20% of subjects were lost to follow-up (Song & Chung, 2010).

d. The evaluation of remaining RFs will be based on a Study Quality (SQ) score. Each study will receive an SQ score, that will act as an overall measure of quality with which studies can be compared. Scores can range from 3-11 as follows.
    i. SQ Score Assignment:
        1. Each study will be given 1-3 points based on the NOS score. Poor-quality studies will be given 1 point, acceptable-quality studies will be given 2 points, and good-quality studies 3 points.

2. A group of top-studied RFs will be established and will include those RFs that are studied in the majority of included studies. Each study will be given 1-4 points based on the percent of top-studied RFs included in the study. Studies with 0-25% of top-studied RFs will be given 1 point, 26-50% will be given 2 points, 51-75% will be given 3 points, and those with 76-100% of top-studied RFs will be given 4 points.
3. Each study will be given 1-4 points based on sample size. Studies with sample sizes of 0-250 will receive 1 point, 251-500 will receive 2 points, 501-750 will receive 3 points, and 750-1,000 will receive 4 points.

ii. For all remaining RFs, the sum of the SQ scores for studies showing predictive value will be compared to the sum of the SQ scores for studies demonstrating lack of predictive value.

1. For RFs in which the sum of SQ scores showing lack of predictive value is greater than the sum of SQ scores showing predictive value, the RF will be eliminated from further review in the primary analysis.
2. For RFs in which the sum of the SQ scores showing predictive value is greater than the sum of the SQ scores

showing lack of predictive value, the RF will be retained for further analysis.

3. In the case of a tie between the sum of the SQ scores showing predictive value and lack of predictive value, the RF will be retained for further analysis.**

iii. The remaining RFs will be assigned an RF score of 3-9 as a means of determining the cumulative value of current evidence regarding each RF.

1. RF Score Assignment:

a. Each RF will be given 1-3 points based on study agreement of predictive value. If 85% or more SQ scores show predictive value, the RF will be given 3 points. If 68-84% of the SQ scores suggest predictive value, the RF will be given 2 points. Finally, if 51-67% of the SQ scores suggest predictive value, the RF will be given 1 point.

b. Each RF will be given 1-3 points based on the percent of the total included studies in which it was reviewed. Those with 0-33% will receive 1 point, 34-66% will receive 2 points, and 67-100% will receive 3 points.

c. Each RF will be given a score of 1-3 based on the average of NOS scores of studies in which the risk factor was studied, where 1 represents low quality and 3 represents high quality.

**At the study start it was unclear whether or not it would be appropriate to attempt a meta-analysis or systematic review only. Given the heterogeneity of included studies, meta-analysis was deemed inappropriate for this set of data (Liberati et al., 2009). Once all data were collected, the specific process of systematic review, described in the above section, was developed under the guidance of SCRS.*

***Ties had not been considered until one occurred. This measure was therefore developed during the factor evaluation process to accommodate ties.*

6. Post Hoc Analysis*

    a. All RFs that were excluded from further analysis will be reconsidered for the purpose of better understanding their role in future research.

        i. RFs in which all studies unanimously agree to lack of predictive value will be eliminated from further analysis.

        ii. The remaining RFs will be given a Modified Risk Factor (MRF) score ranging from 3-9 as a means of determining the cumulative value of current evidence regarding each RF not analyzed in the primary evaluation.

            1. MRF Score Assignment:

                a. Each RF will be given 1-3 points on study agreement of predictive value. RFs showing 35-50% agreement of predictive value based on the

percent SQ score will receive 3 points. RFs showing 16-34% agreement of predictive value will get 2 points. Finally, RFs showing 15% or less agreement of predictive value will get 1 point.

b. Each RF will be given 1-3 points based on the percent of the total included studies in which it was reviewed. Those with 0-33% will receive 3 points, 34-66% will receive 2 points, and 67-100% will receive 1 point. This will assign higher scores to those RFs that have had limited analysis, identifying those in need of further evaluation.

c. Each RF will be given a score of 1-3 based on the average of NOS scores of studies in which the risk factor was studied. In this case those of poor quality will be given a 3 and those of high quality a 1. This will assign higher scores to those RFs that have been assessed using lower-quality study methods, identifying those that may benefit from higher-quality analysis.

**The post hoc analysis was not planned as part of the original study protocol. It was developed during the primary analysis process to better understand the value of risk factors eliminated from further evaluation in the primary analysis.*

7. Results Interpretation Process:
    a. RFs with RF scores of 7-9 will be considered for implications in clinical practice. If there appears to be very little patient risk in assessing the RF, the RF will be recommended as a predictive measure, which should be evaluated by the Nurse Practitioner, in the acute LBP patient.*
        i. Exception: If an RF was studied in only one study, regardless of its RF scores, it will be considered as an RF score of no higher than 6.***
    b. RFs with RF scores of 3-6 will be considered important for future research and strongly recommended to include in future research studies.*
    c. RFs with MRF scores of 7-9 will be considered as likely important for future research and will be recommended to include in future research studies.**
    d. RFs with MRF scores of 3-6 will be considered as possibly being important for future research and will be recommended to include in future research studies.**
    e. RFs with unanimous agreement of lack of predictive value will be considered as having no role in future research.
        i. Exception: If an RF in this category was studied in only one study, it will automatically be considered as having an MRF score of 3-6.***

**Interpretation was developed at time of primary analysis development with help of SCRS.*

***Post hoc interpretation was developed at time of post hoc analysis development.*

****These exceptions were developed during risk-factor evaluation because single-study results were otherwise given more weight than is appropriate for this level of evidence.*

Appendix A References Cited

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