DEVELOPMENT OF A MULTIVARIATE PROGNOSTIC MODEL FOR PAIN AND ACTIVITY LIMITATION IN PEOPLE WITH LOW BACK DISORDERS RECEIVING PHYSIOTHERAPY

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Jon J Ford (PhD)
Low Back Research Team
College of Science, Health & Engineering
La Trobe University Bundoora, Victoria 3085, Australia

Matthew C Richards (BPhysio)
Low Back Research Team
College of Science Health & Engineering, La Trobe University Bundoora, Victoria 3085, Australia
E matt.c.richards@gmail.com

Luke D Surkitt (BPhysio)
Low Back Research Team College of Science
Health & Engineering, La Trobe University Bundoora, Victoria 3085 Australia
E lukesurkitt@gmail.com

Alexander YP Chan (BPhysio)
Low Back Research Team
College of Science, Health & Engineering
La Trobe University Bundoora, Victoria 3085, Australia
E alexanderchan54@gmail.com

Sarah L Slater (PhD)
Low Back Research Team
College of Science, Health & Engineering
La Trobe University Bundoora, Victoria 3085, Australia
E slslater@internode.on.net

Nicholas F Taylor (PhD)
Low Back Research Team
College of Science, Health & Engineering
La Trobe University Bundoora, Victoria 3085, Australia
E N.Taylor@latrobe.edu.au

Andrew J Hahne (PhD)
Low Back Research Team
College of Science, Health & Engineering
La Trobe University Bundoora, Victoria 3085 Australia
E A.Hahne@latrobe.edu.au
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Abstract

Objective: to develop a multivariate prognostic model for back pain, leg pain and activity limitation in patients with early persistent low back disorders.

Design: prospective inception cohort study

Setting: primary care private physiotherapy clinics in Melbourne, Australia

Participants: 300 adults aged 18-65 years with low back and/or referred leg pain of ≥6-weeks and ≤6-months duration

Interventions: not applicable

Main Outcome Measures: numerical rating scales for back pain and leg pain as well as the Oswestry Disability Scale.

Results: prognostic factors included sociodemographics, treatment related factors, subjective/physical examination, subgrouping factors and standardized questionnaires. Univariate analysis followed by generalized estimating equations were used to develop a multivariate prognostic model for back pain, leg pain and activity limitation. Fifty-eight prognostic factors progressed to the multivariate stage where 15 showed significant (p<0.05) associations with at least one of the three outcomes. There were five indicators of positive outcome (two types of low back disorder subgroups, paresthesia below waist, walking as an easing factor and low transversus abdominis tone) and 10 indicators of negative outcome (both parents born overseas, deep leg symptoms, longer sick leave duration, high multifidus tone, clinically determined inflammation, higher back and leg pain severity, lower lifting capacity, lower work capacity and higher pain drawing percentage coverage). The prognostic model explained up to 37% of the variance in outcome.

Conclusion: this study evaluated a comprehensive range of prognostic factors reflective of both the biomedical and psychosocial domains of low back disorders. The multivariate model has potential implications for researchers and practitioners in the field.
Keywords: back pain; predictor; prognosis; physiotherapy

Abbreviations: low back disorders (LBD), numerical rating scale (NRS), Socioeconomic Indices For Areas (SEIFA), health-related quality of life (EuroQol-5D), multivariate generalized estimating equation (GEE)
Introduction

People with recent onset low back disorders (LBD) commonly experience persistence or recurrence of symptoms (1). Identification of prognostic factors has the potential to improve clinical decision making, understanding of disease processes, definitions of risk groups, and prediction of disease outcomes (2). Prognostic factors can also assist in identifying treatment targets to improve treatment effectiveness (3, 4). Recommendations have been made to explore and identify gaps in the prognostic literature for LBD and generate hypotheses for future research (5).

Prognostic studies and systematic reviews on LBD have typically focused on exploration of specific prognostic factors (5, 6) such as psychosocial characteristics (7-10), clinical features (11-14) and measures of physical activity (15). Despite common use by clinicians (16), a comprehensive array of factors reflecting best practice in physiotherapy clinical assessment (17), have not been thoroughly evaluated for prognostic value in LBD. There is also conflicting or limited evidence for prognostic factors based on physical examination (2). There are no high quality studies evaluating a comprehensive range of biomedical (including pathoanatomical), psychological and social prognostic factors using multivariate methods in a sample of people with LBD (4, 18, 19).

This study therefore aimed to develop a multivariate prognostic model for back pain, leg pain and activity limitation in patients with LBD based on a comprehensive range of commonly used prognostic factors reflective of the biopsychosocial model of health.

Methods

Participants, recruitment and treatment

The study was a secondary analysis from a parallel group multi-centre randomized controlled trial (n=300) with participants recruited from metropolitan Melbourne, Australia via public advertisements
and health practitioner referral (20). All participants included in the original trial were also included in the prognostic study analyses. The University Human Ethics Committee approved the trial protocol (21) and written and informed consent was gained for all included participants.

Eligible participants had a primary complaint of low back and/or referred leg pain, had symptom duration of 6-weeks to 6-months, were aged 18-65 years, were fluent in English, belonged to one of five LBD subgroups (Table 1), and agreed to refrain from other treatments during the intervention phase of the trial. Participants were excluded if they had: a current LBD related compensation claim, cancer undergoing treatment, clinical or radiological features of cauda equina syndrome, pregnancy or childbirth (previous 6-months), spinal injections (previous 6-weeks), a history of lumbar spine surgery, a pain intensity score of less than 2 on a 0-10 numerical rating scale (NRS), minimal activity limitation (defined as an ability to walk, sit and stand for at least one hour and no sleep disturbance), received more than five treatments with a trial physiotherapist prior to enrolment, an inability to walk safely (e.g. due to foot drop), and/or planned absence of more than 1-week during the intervention phase of the trial (21).

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Criteria for Membership</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disc herniation with associated</td>
<td>Referred leg symptoms, at least one clinical examination sign suggestive of radiculopathy (positive straight leg raise or reduced lower limb reflexes, sensation, or strength), and computerized tomography or magnetic resonance imaging scan demonstrating a comparable disc herniation</td>
</tr>
<tr>
<td>radiculopathy</td>
<td></td>
</tr>
<tr>
<td>Reducible discogenic pain</td>
<td>At least four out of nine clinical features indicative of discogenic pain and a directional preference in response to repeated or sustained movements/postures (mechanical loading strategies)</td>
</tr>
<tr>
<td>Non-reducible discogenic pain</td>
<td>At least four out of nine clinical features indicative of discogenic pain and an absence of a directional preference in response to mechanical loading strategies</td>
</tr>
<tr>
<td>Zygapophyseal joint pain</td>
<td>At least 3 of the following features: presence of unilateral low back pain, pain reproduction with extension and ipsilateral lateral flexion, localized pain on ipsilateral passive postero-anterior pressure to the transverse process or zygapophyseal joint, and improvement in pain and/or movement following a 1-minute trial of manual therapy directed at the zygapophyseal joint</td>
</tr>
<tr>
<td>Multi-factorial persistent pain</td>
<td>Absence of membership in one of the above pathoanatomical subgroups and an Örebro Musculoskeletal Pain Questionnaire score of greater than 105/210 [7]</td>
</tr>
</tbody>
</table>
Eligible participants were randomized into one of two treatment groups; individualized-physiotherapy incorporating guideline-based advice or advice alone. Nineteen trial physiotherapists provided treatment across 16 centers. Participants allocated to individualized physiotherapy attended 10-sessions of 30-minutes duration. Treatment was individualized according to pathoanatomical, psychosocial and neurophysiological barriers to recovery. This reflects typical clinical practice by physiotherapists and provides clear direction regarding the application of individualized-physiotherapy on the basis of evidence-based and hypothesized causal mechanisms (26, 27). Participants allocated to guideline-based advice attended two 30-minute physiotherapy sessions of guideline-based advice (28). Similar advice was also provided to the participants allocated to individualized-physiotherapy. Full details of the treatment protocols are provided elsewhere (21-25).

Prognostic factors

A wide range of potential prognostic factors were selected based on the foundation text for the physiotherapy assessment of LBD by Geoffrey Maitland (29). Self-administered questionnaires measuring a range of potential prognostic factors were mailed to participants at baseline. Physical examination findings, conducted by a trial physiotherapist at baseline, yielded additional data included as potential prognostic factors. The classification of factors relevant to LBD prognosis is complex with overlapping themes and constructs (27). As such, the potential prognostic factors were categorized based on meaningful labels where possible and also the method of data collection (eg standardized questionnaires).

Sociodemographic factors

Information was recorded regarding age, gender, smoking habits, a range of work-related factors, level of education and parental origin (30). Socioeconomic status was measured via four Socioeconomic Indices For Areas (SEIFA) including Index of Relative Socioeconomic Disadvantage, Index of Education and
Occupation, Index of Economic Resources, and Index of Relative Socioeconomic Advantage and Disadvantage (31-33). The average SEIFA score is 1000 (SD=100) with lower scores representing fewer socioeconomic resources.

_Treatment-related factors_

Potential prognostic indicators related to treatment before commencing the trial included treatment type, medication use and treatment satisfaction. The center/practitioner by which treatment was provided during the trial was also evaluated as a potential prognostic indicator.

_Low back pain-related subjective examination_

A reliable and valid questionnaire for subjective examination was used to record data on: duration, location and nature of symptoms, pain drawing percentage coverage (extent of pain locations), aggravating and easing factors and history of symptoms (30). Clinically determined inflammation was also evaluated and scored positive if three or more of the following symptoms were present: constant symptoms, night-time symptoms most nights despite a firm bed, morning pain or stiffness of at least 60 minutes duration and symptoms easing with movement (34-37).

_Low back pain-related physical examination_

A range of reliable and valid physical examination items (21) were measured including: self reported weight/height, body mass index, posture, response to correcting posture, active movement testing, combined movements, motor control of the local and global muscles, straight leg raise, prone knee bend, lower limb neurological examination, response to mechanical loading strategies, lumbar palpation and response to a “mini-treatment” of lumbar palpation (25).

_Subgroup related factors_

A range of factors were measured relevant to subgrouping of participants independent of above described processes including: features indicative of discogenic pain (24, 38), magnetic resonance or computerized
tomography imaging (for those with clinical radiculopathy) (39) and final subgroup membership (Table 1). The selected subgroups are in common clinical use by medical and allied health providers around the world (16). Detailed descriptions and data supportive of subgroup validity has also been published by a range of research groups (22-25, 40-42). These subgrouping related data were included as potential prognostic indicators.

*Standardized questionnaires*

Overall score as well as individual items from a series of reliable and valid questionnaires were evaluated as potential prognostic factors including the Sciatica Frequency and Bothersomeness Scale (43), the Örebro Musculoskeletal Pain Questionnaire (44), and health-related quality of life (EuroQol-5D) (45). Individual items of the Örebro were intended as screening measures for pain beliefs, activity limitation, psychological distress (eg depression and anxiety), recovery expectations, job satisfaction and fear avoidance beliefs (46).

*Outcome measures*

Self-administered standardized outcome measures were mailed to participants at baseline as well as 5, 10, 26 and 52-weeks post-randomization. These included reliable and valid measures of activity limitation (Oswestry Disability Index (47, 48)), as well as back pain and leg pain measured on numerical rating scales (NRS (49)). Overall score and individual items from the Oswestry were included as potential prognostic factors.

*Statistical analysis*

For the purposes of the RCT, a sample size of 300 was determined a priori based on detecting a between-group difference of 10/100 on the Oswestry, assuming a SD of 20 and 10% loss to follow-up at 12 months (two-tailed hypothesis, α=0.05, power=0.80) and to enable multi-variate analyses of predictors of outcome (21). Multi-phase data analysis (50) was completed comparable with other prognostic studies
In phase 1, univariate analysis was completed to determine which baseline factors were prognostic for activity limitation and pain outcomes over time generally as well as specifically at 5, 10, 26 and 52-weeks following randomization. Categorical and ordinal prognostic factors were dummy coded to enable analysis as clinically relevant dichotomies (53-55). To avoid the recognized issues when using outcome change scores (56) follow-up scores were analysed. Given the large number of potential prognostic factors, univariate linear regression analysis (11, 50, 57, 58) was used to generate unadjusted Pearson correlation coefficients for analysis of association between prognostic factors and outcome at each time point. This process served as a screening process for selection of potentially important variables (51, 52). Considering our relatively large sample size, we applied the guideline of one factor for every five to ten observations (59-61). Redundant and/or overlapping factors were consolidated following author discussion. Multicollinearity was considered likely if factors showed a correlation r>0.8 (62, 63), in which case only one of the correlated factors was chosen for the multivariate analysis. Univariate prognostic factors were then selected to progress to the multivariate analysis based on association with outcome (p<0.05), precedent from other studies and clinical rationale. As we were evaluating prognostic factors independent of treatment provided, treatment group was not included in the analysis as a potential prognostic indicator.

For phase 2 of the analysis, a multivariate generalized estimating equation (GEE) (64) was applied, which accounts for the repeated measures study design (64). All chosen univariate factors from phase 1 were applied to models for each of the three outcomes. A threshold of p>0.1 (65, 66) was used to eliminate clearly insignificant prognostic factors (50). This process generated a list of potential prognostic factors which were then refitted to the final models. Factors with p<0.05 were considered significantly associated with outcome (67, 68).

Relatively low rates of missing data in these factors, and the assumption of data missing at random (69), supported the use of multiple imputation for continuous factors to reduce bias (68, 70, 71). Five imputed data sets were generated including standard errors and confidence intervals reflecting uncertainty of the
imputed values. A pooled estimate was also generated using standard techniques (68, 69). Missing categorical factor data were assigned their own level to determine influence on outcomes.

The limitations of a GEE assuming a linear model are acknowledged with respect to the possibly non-linear nature of LBP recovery over time. However, outcomes were recorded more frequently in the early follow-up period where change would be expected to occur more quickly (baseline, 5 weeks, 10 weeks) to minimise any loss of precision introduced by the use of a linear model.

Sensitivity analysis was conducted to assess the impact of treatment center as a random variable using a generalized linear mixed model (GLMM) (72-74). A complete case analysis examined the difference between the pooled imputed dataset and the dataset without missing values (75). The proportion of variance attributed to the model (57, 62) was assessed by generation of “adjusted R-square” values using linear regression. The statistical software package SPSS (version 21) was used throughout the analysis.

Results

Recruitment occurred between April 28, 2009 and March 30, 2012 with the final 52-week follow up occurring on April 16, 2013. Figure 1 shows the flow of participants through the trial. The main reason for ineligibility was duration of symptoms (n=951). For primary outcomes 292(97%) were followed-up at 10-weeks and 288(93%) at 52-weeks. Baseline characteristics of both groups are presented in Table 2.
Figure 1. Study Flow Diagram
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All participants (n=300)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD) years</td>
<td>43.7 (12.2)</td>
</tr>
<tr>
<td>Female, Number (%)</td>
<td>147 (49%)</td>
</tr>
<tr>
<td>Currently in paid employment, Number (%)</td>
<td>230 (77%)</td>
</tr>
<tr>
<td>Referred leg pain below knee, Number (%)</td>
<td>142 (47%)</td>
</tr>
<tr>
<td>Duration of back pain, mean (SD) weeks</td>
<td>15.4 (10.6)</td>
</tr>
<tr>
<td>Duration of leg pain, mean (SD) weeks</td>
<td>10.5 (9.9)</td>
</tr>
<tr>
<td>Sciatica Frequency Scale, mean (SD)</td>
<td>14.3 (6.1)</td>
</tr>
<tr>
<td>Sciatica Bothersomeness Scale, mean (SD)</td>
<td>13.7 (6.1)</td>
</tr>
<tr>
<td>Örebro Musculoskeletal Pain Questionnaire, mean (SD)</td>
<td>97.7 (24.5)</td>
</tr>
<tr>
<td>Quality of life (EuroQol-5D utility score), mean (SD)</td>
<td>0.6 (0.2)</td>
</tr>
<tr>
<td>Interference with work/housework in the past week, mean (SD)</td>
<td>2.1 (1.1)</td>
</tr>
<tr>
<td>Number of work days missed in the last 30 days, mean (SD)</td>
<td>2.5 (6.5)</td>
</tr>
<tr>
<td><strong>Subgroup membership, Number (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Disc herniation with associated radiculopathy</td>
<td>54 (18%)</td>
</tr>
<tr>
<td>Reducible discogenic pain</td>
<td>78 (26%)</td>
</tr>
<tr>
<td>Non-reducible discogenic pain</td>
<td>96 (32%)</td>
</tr>
<tr>
<td>Zygapophyseal joint pain</td>
<td>64 (21%)</td>
</tr>
<tr>
<td>Multi-factorial persistent pain</td>
<td>8 (3%)</td>
</tr>
<tr>
<td><strong>Primary outcomes, mean (SD)</strong></td>
<td></td>
</tr>
<tr>
<td>Oswestry</td>
<td>29.4 (12.3)</td>
</tr>
<tr>
<td>Back pain intensity on NRS</td>
<td>5.4 (1.9)</td>
</tr>
<tr>
<td>Leg pain intensity on NRS</td>
<td>4.7 (2.7)</td>
</tr>
</tbody>
</table>

Abbreviations: Oswestry, Oswestry Disability Index (ten item questionnaire scored out of 100%); NRS, numerical pain rating scale (scored from 0-10). Sciatica Frequency and Bothersomeness Scales (five items for both frequency and bothersomeness) scored out of 30, Örebro Musculoskeletal Pain Questionnaire (21 items) scored out of 210, EuroQol-5D (five items) scored between -0.594 to 1.0, and interference with work/housework scored on a five point scale.

**Table 2: Baseline characteristics of participants**
Fifty-eight prognostic factors including categorical and ordinal dummy levels from the univariate analysis progressed to the multivariate stage (Supplementary Digital Content). Multivariate analysis initially identified 19 baseline factors (24 levels) that satisfied the set p-value threshold of 0.1 for at least one outcome. Each of these factors contained less than 8% missing data. Results of the refitted GEE over time generally for these final 19 factors are presented in Table 3. Fifteen factors (18 levels) showed significant (p<0.05) associations with at least one of the three outcomes. Reducible discogenic (positive factor), both parents born overseas (negative factor), each of the 10, 26 and 52-week time points (positive factor) and pain drawing percentage coverage (negative factor) were significant for all outcomes.

The results of the GLMM were generally consistent with the GEE. However, zygapophyseal joint subgroup, transversus abdominis low tone and general health were significantly associated with leg pain outcome using the GLMM but not the GEE. On the back pain outcome, inflammation and pain drawing percentage area were significant with the GEE but not with the GLMM.

The complete case analysis results were similar to the GEE. However, clinical inflammation (for Oswestry) and lateral flexion (for Oswestry and leg pain) were significant with the complete case analysis but not the GEE. Despite being significant with the GEE, disc herniation/radiculopathy subgroup (for back pain), reducible discogenic pain subgroup and sick leave (both for Oswestry) and both parents born overseas (for leg pain) were not significant with complete case analysis.
<table>
<thead>
<tr>
<th>Prognostic factor</th>
<th>N</th>
<th>B Coefficient (95% CI)</th>
<th>p-value</th>
<th>N</th>
<th>B Coefficient (95% CI)</th>
<th>p-value</th>
<th>N</th>
<th>B Coefficient (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td></td>
<td>-0.2(-14.4 to 13.9)</td>
<td>.975</td>
<td></td>
<td>0.0(-1.962 to 2.019)</td>
<td>.977</td>
<td></td>
<td>-2.0(-4.3 to 0.4)</td>
<td>.095</td>
</tr>
<tr>
<td>Subgroup</td>
<td>54</td>
<td>-1.3(-5.0 to 2.3)</td>
<td>.473+</td>
<td>54</td>
<td>-0.6(-1.2 to -0.1)</td>
<td>.029+</td>
<td>54</td>
<td>-0.3(-0.9 to 0.3)</td>
<td>.312+</td>
</tr>
<tr>
<td>Disc herniation/ radiculopathy*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reducible discogenic pain*</td>
<td>78</td>
<td>-3.2(-5.9 to -0.6)</td>
<td>.017+</td>
<td>78</td>
<td>-0.9(-1.3 to -0.4)</td>
<td>&lt;.001+</td>
<td>70</td>
<td>-0.7(-1.2 to -0.2)</td>
<td>.005+</td>
</tr>
<tr>
<td>Manual therapy group*</td>
<td>64</td>
<td>-2.6(-5.5 to 0.3)</td>
<td>.082+</td>
<td>64</td>
<td>-0.5(-1.0 to 0.0)</td>
<td>.050+</td>
<td>49</td>
<td>-0.2(-0.7 to 0.4)</td>
<td>.560+</td>
</tr>
<tr>
<td>Multifactorial persistent pain*</td>
<td>8</td>
<td>-1.3(-7.8 to 5.1)</td>
<td>.683+</td>
<td>8</td>
<td>0.2(-0.5 to 0.8)</td>
<td>.647</td>
<td>7</td>
<td>-0.2(-1.4 to 0.9)</td>
<td>.725+</td>
</tr>
<tr>
<td>Parents born overseas</td>
<td>165</td>
<td>3.4(1.1 to 5.7)</td>
<td>.004</td>
<td>165</td>
<td>0.6(0.2 to 0.9)</td>
<td>.003</td>
<td>141</td>
<td>0.5(0.1 to 0.9)</td>
<td>.026</td>
</tr>
<tr>
<td>Both born overseas#</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One born overseas#</td>
<td>21</td>
<td>0.7(-3.7 to 5.1)</td>
<td>.761</td>
<td>21</td>
<td>0.2(-0.4 to 0.8)</td>
<td>.570</td>
<td>18</td>
<td>0.1(-0.5 to 0.8)</td>
<td>.723</td>
</tr>
<tr>
<td>Paresthesia below waist</td>
<td>134</td>
<td>-3.3(-6.0 to -0.6)</td>
<td>.016+</td>
<td>134</td>
<td>-0.1(-0.5 to 0.3)</td>
<td>.607+</td>
<td>125</td>
<td>-0.2(-0.6 to 0.3)</td>
<td>.498+</td>
</tr>
<tr>
<td>Deep leg symptoms</td>
<td>145</td>
<td>2.5(0.0 to 4.9)</td>
<td>.053</td>
<td>145</td>
<td>0.2(-0.2 to 0.6)</td>
<td>.286</td>
<td>145</td>
<td>0.6(0.2 to 1.0)</td>
<td>.002</td>
</tr>
<tr>
<td>Walking eases symptoms</td>
<td>160</td>
<td>-2.0(-4.2 to 0.2)</td>
<td>.073+</td>
<td>160</td>
<td>-0.5(-0.9 to -0.2)</td>
<td>.005+</td>
<td>138</td>
<td>-0.2(-0.6 to 0.2)</td>
<td>.273+</td>
</tr>
<tr>
<td>Lateral flexion limited by pain</td>
<td>116</td>
<td>1.0(-1.3 to 3.4)</td>
<td>.382</td>
<td>116</td>
<td>0.1(-0.3 to 0.5)</td>
<td>.536</td>
<td>106</td>
<td>0.4(0.0 to 0.8)</td>
<td>.055</td>
</tr>
<tr>
<td>Transversus abdominis low tone</td>
<td>109</td>
<td>-3.0(-5.3 to -0.7)</td>
<td>.012+</td>
<td>109</td>
<td>-0.8(-1.1 to -0.4)</td>
<td>&lt;.001+</td>
<td>91</td>
<td>-0.4(-0.9 to 0.0)</td>
<td>.051</td>
</tr>
<tr>
<td>Multifidus high tone</td>
<td>60</td>
<td>2.0(-1.2 to 5.1)</td>
<td>.215</td>
<td>60</td>
<td>0.0(-0.4 to 0.5)</td>
<td>.918</td>
<td>47</td>
<td>0.7(0.1 to 1.4)</td>
<td>.019</td>
</tr>
<tr>
<td>Clinical inflammation</td>
<td>182</td>
<td>1.1(-1.1 to 3.3)</td>
<td>.342</td>
<td>182</td>
<td>0.4(0.1 to 0.8)</td>
<td>.020</td>
<td>165</td>
<td>-0.2(-0.6 to -0.2)</td>
<td>.311+</td>
</tr>
<tr>
<td>Time points</td>
<td>300</td>
<td>-3.6(-4.8 to -2.4)</td>
<td>&lt;.001+</td>
<td>300</td>
<td>-0.4(-0.6 to -0.1)</td>
<td>.001+</td>
<td>261</td>
<td>-0.5(-0.8 to -0.3)</td>
<td>&lt;.001+</td>
</tr>
<tr>
<td>10-week time point^</td>
<td>300</td>
<td>-5.5(-6.9 to -4.2)</td>
<td>&lt;.001+</td>
<td>300</td>
<td>-0.5(-0.7 to 0.3)</td>
<td>&lt;.001+</td>
<td>261</td>
<td>-0.7(-1.0 to -0.4)</td>
<td>&lt;.001+</td>
</tr>
<tr>
<td>26-week time point^</td>
<td>300</td>
<td>-7.8(-9.4 to -6.2)</td>
<td>&lt;.001+</td>
<td>300</td>
<td>-0.8(-1.0 to -0.5)</td>
<td>&lt;.001+</td>
<td>261</td>
<td>-0.9(-1.2 to -0.6)</td>
<td>&lt;.001+</td>
</tr>
<tr>
<td>52-week time point^</td>
<td>300</td>
<td>-7.8(-9.4 to -6.2)</td>
<td>&lt;.001+</td>
<td>300</td>
<td>-0.8(-1.0 to -0.5)</td>
<td>&lt;.001+</td>
<td>261</td>
<td>-0.9(-1.2 to -0.6)</td>
<td>&lt;.001+</td>
</tr>
<tr>
<td>Back pain severity</td>
<td>300</td>
<td>0.2(-0.5 to 0.8)</td>
<td>.556</td>
<td>300</td>
<td>0.3(0.2 to 0.4)</td>
<td>&lt;.001</td>
<td>261</td>
<td>0.1(0.0 to 0.2)</td>
<td>.245</td>
</tr>
<tr>
<td>Leg pain severity</td>
<td>300</td>
<td>0.1(-0.5 to 0.6)</td>
<td>.764</td>
<td>300</td>
<td>0.0(-0.1 to 0.1)</td>
<td>.896</td>
<td>261</td>
<td>0.3(0.2 to 0.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Prognostic Factor</td>
<td>B-coefficient</td>
<td>p-value</td>
<td>B-coefficient</td>
<td>p-value</td>
<td>B-coefficient</td>
<td>p-value</td>
<td></td>
<td></td>
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<td>------------------------------------------</td>
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<td></td>
</tr>
<tr>
<td>Örebro sick leave duration (0-10)</td>
<td>1.1(0.4 to 1.7)</td>
<td>.002</td>
<td>0.1(0.0 to 0.2)</td>
<td>.112</td>
<td>0.1(0.0 to 0.2)</td>
<td>.219</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Örebro light work capacity (0-10)</td>
<td>1.2(0.5 to 1.8)</td>
<td>&lt;.001</td>
<td>0.0(-0.1 to 0.1)</td>
<td>.996</td>
<td>0.1(0.0 to 0.2)</td>
<td>.099</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Örebro shopping capacity (0-10)</td>
<td>0.4(-0.2 to 1.1)</td>
<td>.186</td>
<td>0.1(0.0 to 0.2)</td>
<td>.104</td>
<td>0.0(-0.1 to 0.1)</td>
<td>.519+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain drawing area (0-100)</td>
<td>0.2(0.0 to 0.3)</td>
<td>.006</td>
<td>0.0(0.0 to 0.0)</td>
<td>.042</td>
<td>0.0(0.0 to 0.1)</td>
<td>.005</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oswestry lifting (0-10)</td>
<td>2.4(1.4 to 3.5)</td>
<td>&lt;.001</td>
<td>0.1(-0.1 to 0.2)</td>
<td>.441</td>
<td>0.3(0.1 to 0.5)</td>
<td>.007</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lateral flexion range limitation</td>
<td>0.2(0.0 to 0.4)</td>
<td>.069</td>
<td>0.0(0.0 to 0.0)</td>
<td>.259</td>
<td>0.0(0.0 to 0.1)</td>
<td>.241</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General health (0-100)</td>
<td>0.0 (0.0 to 0.1)</td>
<td>.278</td>
<td>0.0(0.0 to 0.0)</td>
<td>.420</td>
<td>0.0(0.0 to 0.0)</td>
<td>.085</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quality of life</td>
<td>-3.7(-10.7 to 3.3)</td>
<td>.300+</td>
<td>-0.9(-1.9 to 0.1)</td>
<td>.077+</td>
<td>0.1(-1.0 to 1.3)</td>
<td>.833</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

R-squared 0.37 0.30 0.34

*relative to “non-reducible discogenic pain”, #relative to "both parents born in Australia", ^relative to "5-week time point", +Positive prognostic indicator
Results are independent of time point, significant p-values in bold. Negative B-coefficients represent lower outcome scores and therefore a better outcome at follow-up in participants with the listed prognostic factor. Predicted outcome for a given patient can be calculated by applying the patient’s score on each baseline factor to the B-coefficients, and adding the scores from each item together (including the intercept)

Table 3: Prognostic factors for Oswestry, back pain and leg pain obtained from the multivariate model
Discussion

This study identified five indicators of positive outcome (belonging to either the reducible discogenic pain or disc herniation/radiculopathy subgroups, paresthesia below waist, walking as an easing factor and low transversus abdominis tone) and 10 indicators of negative outcome (both parents born overseas, deep leg symptoms, higher Örebro sick leave duration, high multifidus tone, clinically determined inflammation, higher back and leg pain severity, lower Oswestry lifting capacity, lower Örebro light work capacity and higher pain drawing percentage coverage). The multivariate model explained 30-37% of the variance depending on the outcome evaluated. This study is unique in evaluating a comprehensive range and commonly used set of prognostic factors reflective the biomedical, psychological and social domains. The multivariate model therefore has potential implications for researchers and practitioners in the field.

Researchers and clinical practice guidelines (76) have suggested that biomedical factors are not relevant in clinical decision making beyond the identification of red flags (26) and few studies have identified biomedical or physical factors of prognostic value (77). However biomedical factors are commonly used by clinicians in decision making (16). Our study has identified that nine of the 15 prognostic factors related primarily to pathoanatomical mechanisms. Reducible discogenic pain is a partially validated subgroup of LBP, where repeated or sustained movements/postures result in centralization or peripheralization of pain. This phenomenon has been hypothesized as being due to migration of the nucleus pulposus within the annulus fibrosis (24). Treatment based on this mechanism can result in rapid improvement (78) which may be why the reducible discogenic pain subgroup was found as a positive prognostic factor; an observation with some support from other studies (79).

Previously, disc herniation and distal leg symptoms have been identified as negative prognostic indicators (5). This contrasts with our results where these factors were positive prognostic indicators. This finding could potentially be due to our reference category being the non-reducible discogenic pain group where outcomes were worse than for the disc herniation with radiculopathy group. Alternatively in the context
of a comprehensive multivariate model participants with DHR may in fact have a more positive prognosis potentially related to unique mechanisms of healing such as resorption of herniated disc material (80).

There is emerging evidence on the validity of clinically determined inflammation as measured by features such as constancy of symptoms and 24 hour symptom behavior (35, 81). However, our study is the first we are aware of that demonstrates clinical inflammation as a prognostic indicator of negative outcome. Excessive and prolonged inflammatory processes may be a mechanism of delayed LBD recovery (80, 82). Our observations are consistent with other research showing low transversus abdominis tone as a prognostic indicator of positive outcome (83, 84). These results support the notion that variation in the pattern of motor control strategy in individuals is important in determining individualized treatment. However the mechanisms underpinning our findings on motor control, including high multifidus tone as a negative prognostic indicator, are complex, yet to be fully determined and controversial (85).

The psychosocial and demographic factors most commonly associated with poor prognosis (5) such as counterproductive beliefs, work factors, age, psychological stress and poor general health were not found to be independent prognostic factors within the context of a comprehensive multivariate model. Previous research has found that pain drawing percentage coverage (extent of pain locations of a self administered body chart) is not a consistent prognostic factor (86, 87) but our data suggest that the role of this simple tool as a marker of pain focus should be reconsidered. The prognostic impact of parental origin is likely related to genetic and environmental influences (88) and requires further investigation as an indicator of negative outcome. Severity of baseline outcome measures such as pain, activity limitation and sick leave have been consistently shown as prognostic indicators of negative outcome (77) and our study supports these findings.

Much of the research on prognostic factors for LBP has been reported to be of low quality (2, 77). The strengths of the current study include selection of a prospective, clearly defined and representative sample, low loss to follow up, use of predominantly reliable and valid measures of prognosis/outcomes,
use of a comprehensive range of factors representative of a biopsychosocial approach within a multivariate model, and appropriate statistical analysis (89). We have addressed all items recommended on reporting of prognostic studies in the TRIPOD Checklist (90).

**Study limitations**

There are some limitations including insufficient validation for some measures used as potential prognostic factors. For example motor control was determined by clinical observation that is commonly used but not validated against a suitable reference standard. The prognostic model explained 30-37% of the variance in outcome, suggesting other factors not accounted for in our study may have contributed to outcomes. However our analysis used data from a randomized controlled trial where substantial additional variance may have been attributable to the significant between-group effects. We did not include treatment group in the models, nor did we evaluate results for each treatment separately, as we were seeking to identify predictors that would be generalizable to a range of conservative treatments. Predictors of preferential treatment effects (effect modifiers) will be reported separately. Our analyses across a range of time points may further reduce the variance accounted for, but this approach also increases generalizability of the model. Although we measured the psychological domain using a well accepted screening tool (91), it is possible that a larger amount of variance due to psychological factors would have been explained by more specific diagnostic measures.

**Conclusion**

A 15-factor prognostic model was developed from a comprehensive range of clinically assessed variables in accordance with a biopsychosocial model. These data and the potential mechanisms underpinning the model support the importance of biomedical factors within the context of a biopsychosocial approach. Researchers and practitioners should consider these prognostic factors with reference to validating and providing individualized treatment for people with LBD. Further high quality research is required to externally validate these findings and explore potential mechanisms of effect.
References


