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Risk factors for low back pain outcome: Does it matter when they are measured?

David Murray Klyne[1] | **Leanne Marie Hall**[1] | **Michael K. Nicholas**[2] | **Paul William Hodges**[1]

[1]NHMRC Centre of Clinical Research Excellence in Spinal Pain, Injury and Health, School of Health and Rehabilitation Sciences, The University of Queensland, Brisbane, Australia

[2]Pain Management Research Institute, Royal North Shore Hospital, The University of Sydney, Sydney, Australia

Correspondence
Paul Hodges, School of Health and Rehabilitation Sciences, The University of Queensland, Brisbane QLD, Australia 4072, Australia.
Email: p.hodges@uq.edu.au

Abstract

Background: The early identification of factors that increase risk of poor recovery from acute low back pain (LBP) is critical to prevent the transition to chronicity. Although most studies of risk factors for poor outcome in LBP tend to investigate the condition once it is already persistent, there is evidence to suggest that this differs from risk factors measured during the early-acute stage. This study aimed to identify early risk factors for poor outcome in the short- and long-term in individuals with acute LBP, and to compare this with factors identified at 3 months in the same cohort.

Methods: One hundred and thirty-three individuals were recruited within 2 weeks of an acute LBP episode and completed questionnaires related to their sociodemographic, psychological, clinical and history/treatment status at baseline and 3 months later, and their pain-level fortnightly for 12 months.

Results: Of the 133 participants recruited, follow-up data were provided by 120 at 3 months, 97 at 6 months, 85 at 9 months and 94 at 12 months. Linear regression identified various factors at baseline (acute phase) and 3 months later that predicted short- and long-term outcome (pain level, change in pain). Key findings were that: (1) depressive symptoms at baseline most consistently predicted worse outcome; (2) psychological factors in general at 3 months were more predictive of outcome than when measured at baseline; (3) early health care utilization predicted better outcome, whereas use of pain medication later (3 months) predicted worse outcome; and (4) sex and BMI predicted outcome inconsistently over 12-months.

Conclusions: The results highlight the multidimensional nature of risk factors for poor outcome in LBP and the need to consider time variation in these factors.

Significance: This study attempts to consider the impact of time variation of candidate risk factors on long-term outcome from the very early onset of acute low back pain. Risk factors across domains (sociodemographic, psychological, clinical, history/treatment) were identified, but their relationship with outcome often depended on when (acute phase *vs.* 3 months later) they were measured after back pain onset. Findings highlight the need to consider both a diverse range of factors and their potential time variance when assessing risk of poor outcome.

1 | INTRODUCTION

Low back pain (LBP) is a leading cause of disability (James et al., 2017) and health-related economic burden (Dagenais et al., 2008) internationally. The majority of this burden is associated with the transition to a persistent or recurrent condition, but attempts to prevent this transition have had limited impact. Identification of factors that may contribute to a poor prognosis is a major research goal to provide potentially modifiable targets to reduce the burden of LBP. A diverse range of factors have been studied across sociodemographic (e.g., age, sex, education and employment status) (Burton et al., 1995; Campbell et al., 2013; Pincus et al., 2008), psychological (depression, pain catastrophizing and self-efficacy) (George & Beneciuk, 2015; Jegan et al., 2017; Pincus et al., 1976, 2006) and clinical (e.g., pain/disability intensity and duration) (Campbell et al., 2013; Henschke et al., 2008; Klyne et al., 2019) domains. Most studies of risk factors in LBP consider few (generally short-term) follow-up periods, and study individuals when the condition has become established beyond the acute phase. This is problematic for two reasons. First, studies of LBP trajectory are beginning to show that for most, LBP is an ongoing condition marked by fluctuating symptoms (Dunn et al., 2013; Kongsted et al., 2015), which cannot be captured without frequent and long-term assessments. Second, risk factors for poor outcome (i.e., persistent pain) may differ depending on whether the LBP is a new acute episode or an ongoing problem.

Risk factors for poor long-term outcome in LBP are largely psychosocial (Foster et al., 2010; Linton, 1976; Pincus et al., 1976). Although it is likely that risk factors for the transition from acute-to-persistent LBP will overlap with those which maintain it, longitudinal studies of acute LBP have also begun to identify differences. For instance, fear of pain is a strong predictor of poor outcome in people already experiencing persistent LBP, but not in those with LBP of <3 months duration (Grotle et al., 2010). Similarly, fear avoidance was a stronger predictor of outcome in chronic than acute (<3 weeks since onset) LBP, whereas emotional distress and sociodemographic factors explained more of the variation in outcome in those with acute LBP (Grotle et al., 2006). These differences are not reported universally – a study of primary care patients reported no differences in prognostic factors between those with acute/subacute (<3 months since onset) and chronic LBP in the prediction of disability 12 months later (Grotle et al., 2010). A major issue for interpretation of this research is that the exposure to risk factors is not static and can change over time. For instance, higher depressive symptoms more strongly predict worse outcome during the acute than chronic phase of LBP (Burton et al., 1995). To understand the impact of time variation in risk factors on LBP, it is necessary to investigate risk factors earlier during the acute phase of LBP, more frequently, and over longer periods.

This study aimed to identify sociodemographic, psychological, clinical and history (i.e., previous LBP)/treatment (or non-treatment) risk factors for poor outcome (pain) in the short- and long-term from measurements made in individuals with early-acute LBP, and to compare this with risk factors identified from measurements made in the same cohort 3 months later – the point at which, by definition, acute pain is defined to become chronic (Treede et al., 2015).

2 | METHODS

2.1 | Participants

This study analysed data from a data-intensive cohort study that included extensive collection of biological, behavioural, psychological and social data from individuals who were recruited within 2 weeks of onset of an acute episode of LBP and followed for 12 months (Klyne et al., 2020). This analysis involved data from the entire cohort of 133 participants. Participants were recruited through advertisements around the University campus and local community, social media, three nearby hospitals and via a professional recruitment agency. Ethical clearance was obtained from the Institutional Human Research Ethics Committees and the recruiting hospitals. All participants provided informed consent, and were remunerated $50 AUD on study commencement and $150 AUD on study completion 12 months later. Some analyses of other data (i.e., laboratory-based biological measures) from this participant cohort have been reported previously (e.g., Alshehri et al., 2021; Klyne et al., 2017, Klyne, Barbe, et al., 2018, Klyne, Moseley, et al., 2018, 2019, Klyne, Barbe, Hodges, 2021, Klyne, Barbe, James, et al., 2021; Klyne & Hodges, 2020)).

Participants were recruited and assessed within 2 weeks of onset of an acute episode of LBP that was preceded by at least 1 month without pain. To ensure participants had experienced an acute LBP episode of sufficient duration and intensity, we employed a two-phase screening process with respect to pain and disability (Klyne et al., 2020). Initially, participants were screened by an automated online screening questionnaire that included participants if their LBP (1) occurred within the last 2 weeks and lasted for at least 24 hours, (2) caused functional limitation and (3) caused them to seek/seriously consider health intervention. Then, within 24 hours of starting the study, potential participants were only included if their LBP intensity and LBP-related disability exceeded a minimum average

threshold level of ≥1/10 and ≥1/28, respectively, for the week prior to the initial assessment. LBP was assessed using a numerical rating scale (NRS) anchored with 'no pain' at 0 and 'worst pain imaginable' at 10, in response to the question: 'Please give a number to describe your average pain over the past week.' LBP-related disability was assessed using the Roland Morris Disability Questionnaire (RMDQ) (Roland and Morris 1983), with a total range score of 0 (no disability) to 28 (severe disability).

Participants were excluded if they were <18 or >50 years old, had a confirmed or suspected serious spinal pathology, had major pain or injury to other body regions in the previous 12 months or had other known major diseases or disorders (e.g., chronic renal/endocrine disorders, heart/coronary artery disease, cancer, and major progressive neurological disorders such as multiple sclerosis and muscular dystrophy). To control factors that might influence inflammatory-related pain, participants were also excluded if they were using corticosteroids or anti-cytokine therapy (Carp et al., 2007). Participants were allowed to use pain medications that do not affect inflammatory cytokines (i.e., simple analgesics such as paracetamol), and, if required, could use non-steroidal anti-inflammatory pain medication (e.g., Ibuprofen) provided it ceased 5 days prior to completing assessments at each 3-month assessment time point.

2.2 | Data collection overview

Analysis was conducted on sociodemographic, psychological, clinical and LBP history/treatment data that were collected at two time points: baseline (within 2 weeks of LBP onset) and 3 months later. Data pertaining to the participant's 'average' level of LBP and LBP-related disability were collected each fortnight for 12 months. All data were collected via online questionnaires that were emailed to participants. If participants did not complete the questionnaires within 24 hours of the initial email request, an automatic email reminder was sent every day for 7 days for the fortnightly questionnaires, and every day for 2 weeks for the 3-monthly questionnaires. If a participant missed one or more of the 3-monthly questionnaire assessments, they were still invited to complete the final questionnaire at 12 months.

2.3 | Measures

2.3.1 | Pain and disability as clinical factors and outcomes measures

Measures of pain (NRS) and disability (RMDQ; see section 2.1) were both considered as potential *risk factors* (clinical factors), whereas pain alone was used to generate the primary *outcome measures*. As candidate risk factors, one-off pain and disability scores were used at baseline, and the average of the fortnightly scores for the last month at the 3-monthly assessment time point (i.e., scores at weeks 8, 10 and 12) were calculated to represent the participants' pain and disability status at 3 months.

As an outcome measure, the participants' pain was expressed in two ways: (1) average level of pain over the last month (pain level, as calculated above), and (2) the change in pain from baseline (pain change). For *pain level*, fortnightly pain scores (NRS) for the last month at each 3-monthly assessment time point were averaged to represent the participants' pain level at 3, 6, 9 and 12 months. *Pain change* was expressed as the change in the participants' pain level from baseline (at 3, 6, 9 and 12 months, separately) as a proportion of the summed pain level for the two time points, which resulted in a score that ranged between −1.0 and 1.0. This method removes the bias towards greater increases than decreases from baseline that would occur with percentage change calculations (e.g., a change in pain from 2 to 8 would equate to a 300% increase, whereas a change in pain from 8 to 2 equates to a 75% decrease). A score <0 indicates a decrease in pain from baseline, a score >0 indicates an increase and a score of 0 meant that pain was unchanged from baseline.

2.3.2 | Sociodemographic factors

Age and gender were recorded. Body mass index (BMI) was calculated from the participants' self-reported height and weight. Cigarette smoking status was dichotomized as 'previous or current smoker' or 'non-smoker'. Marital status was dichotomized as 'not married/cohabitating' (never married, separated, divorced, widowed) or 'married or cohabitating' (married, cohabitating). Education level was dichotomized as 'low' (primary or upper secondary education) or 'high' (vocational education/training, higher education/university). Employment status was dichotomized as 'unemployed' (unemployed, unemployed but retraining, not seeking employment) or 'employed' (full time, part time). Whether there was any impending compensation associated with the participants' LBP was dichotomized as 'yes' or 'no'.

2.3.3 | History/treatment factors

Participants self-reported their LBP history, health care and pain medication usage for their LBP. LBP history was dichotomized as either having had a previous episode of LBP (at baseline) or not. Health care use (e.g.,

physiotherapy, chiropractor, general practitioner) and pain medication use were both dichotomized as either 'yes' or 'no'.

2.3.4 | Psychological factors

We selected measures of psychological variables with satisfactory psychometric properties that considered the three key domains of relevance in LBP: cognitive (expectations, beliefs and perceptions concerning pain) (Boersma & Linton, 2005; Henschke et al., 2008; Linton, 1976; Mallen et al., 2007), emotional (distress, anxiety and depression) (Pincus et al., 1976) and behavioural (coping, pain behaviour and activity/activity avoidance) (Henschke et al., 2008; Linton, 1976; Mallen et al., 2007). The 20-item Center for Epidemiological Studies Depression Scale (CES-D, range: 0–60) was used to assess depressive symptoms in the past week (Radloff, 1977). Higher scores represent higher levels of symptoms, and scores >15 are indicative of high risk for clinical depression (Lewinsohn et al., 1997). The 13-item Pain Catastrophizing Scale (PCS, range: 0–52) was used to assess the presence of catastrophic thought processes related to pain without reference to a time point (Osman et al., 1997). Higher scores imply greater pain catastrophizing. The 11-item Fear Avoidance Beliefs Questionnaire (FABQ) was used to assess fearful and avoidant behaviours related to physical activity (FABQ-PA; 4 items; range: 0–24) and work (FABQ-W; 7 items; range: 0–42) attributed to the participants' LBP, again without reference to a time point (Waddell et al., 1993). Higher scores reflect stronger fear-avoidance beliefs. Unemployed participants were not included in the final FABQ-W dataset. The 10-item Pain Self-Efficacy Questionnaire (PSEQ, range: 0–60) was used to assess the confidence participants had in performing activities while in pain at present (Nicholas, 2007). Higher scores imply a greater confidence in the ability to do things despite pain.

2.4 | Statistics

Descriptive statistics for the entire sample were generated for all variables at baseline. Independent *t* tests (continuous variables) and chi-square statistics (categorical variables) were used to compare variables between participants who did and did not provide follow-up data at 3, 6, 9 and 12 months.

Identification of the factors at baseline (i.e., during acute LBP) that predict outcome (i.e., *pain level* and *pain change*, separately) was assessed using a sequential regression analysis approach separately for outcomes at 3, 6, 9 and 12 months. First, univariate linear regression was used to determine the regression coefficient for each baseline factor separately in relation to each outcome measure at a specific 3-month time point. Second, all factors with a *P*-value of <0.05 at this stage were considered a *predictor* and retained for examination within domains of 'sociodemographic', 'clinical', 'history/treatment' and 'psychological' using multivariable regression analysis. Domains were chosen to manage the large number of variables in the data set, and to extract the predictor(s) that best explain the association with outcome from each respective domain. As there is overlap between many variables related to pain (especially psychological (Pincus et al., 1976)), this approach accounted for potential intercorrelation between variables and thus enabled identification of the key predictor(s) for each domain (Campbell et al., 2013). Third, all non-significant predictors ($p > 0.05$) in each domain-specific model were removed and the remaining predictors were entered into a final multivariable model for outcomes at the specific 3-month time point. To address the second aim of the study, the same three-step approach was used to identify factors at 3 months (post LBP onset) that predict outcomes at 6, 9 and 12 months.

Because of the large number of variables with potential to correlate with one another, which can lead to incorrect inferences about relationships between predictor and outcome variables (Vatcheva et al., 2016), we checked for collinearity between variables included in each of the multivariable models. This was assessed by using the Variance Inflation Factor (VIF), which measures how much the variance of a coefficient is 'inflated' because of its relationship with one or more predictors (Zuur et al., 2010). All VIF scores were <1.84, which is well below that considered evidence of multicollinearity (≥5) (Craney & Surles, 2002). Analyses were performed using GraphPad Prism v12 (San Diego, California) and Stata v14 (StataCorp, College Station, Texas). *p*-values <0.050 were considered statistically significant.

3 | RESULTS

3.1 | Baseline characteristics

Baseline characteristics are summarized in Table 1, with delineation for those who did and did not provide follow-up data at 3 (total lost to follow-up =13, 9.8%), 6 (total lost to follow-up = 36, 27.1%), 9 (total lost to follow-up = 48, 36.1%) and 12 (total lost to follow-up =39, 29.3%) months. All participants were invited to complete questionnaires at 12 months irrespective of whether or not they had continued or failed to return for follow-up earlier, reflecting the lower attrition at 12 than 9 months. Although

baseline characteristics were generally similar (59 of the 72 comparisons were not different) between follow-up and non-follow-up participants, there were some differences. Lower incidence of previous LBP, higher pain and higher disability were reported by participants who did than did not follow-up at 3, 6 and 12 months, respectively. Regarding psychological factors, higher pain catastrophizing was reported by those that did not follow up at 6 and 12 months, and higher depressive symptoms along with lower pain self-efficacy were reported by those that did not follow-up at any time point.

Characteristics were consistent with other acute/subacute LBP cohorts (Grotle et al., 2010; Tan et al., 2018), with moderately high pain levels (Boonstra et al., 2014) but low disability and psychosocial symptoms relative to chronic LBP (Doualla et al., 2019; Grotle et al., 2010; Mutubuki et al., 2020). That most participants had previously experienced LBP is consistent with the high (~85%) lifetime prevalence of LBP in the general population (Manchikanti, 2000; Walker, 2000).

3.2 | Sociodemographic predictors

At baseline, univariate tests showed that a greater BMI predicted lower pain (pain level) and reduced pain (pain change) from baseline at 3 and 12 months. Conversely, impending compensation predicted higher pain at 9 months, and being female predicted both higher and increased pain from baseline at 12 months. In the multivariable models of *sociodemographic* factors, all factors (BMI, sex, pending compensation) remained predictive of pain level, but only BMI remained predictive of the change in pain (Tables 2–5).

For measures made at 3 months, sex (female) predicted higher pain and an increase in pain at 12 months, and impending compensation predicted higher pain at 9 months (Tables 6 and 7). As no other sociodemographic factors at 3 months were predictive of outcome (at the same time point), no multivariable modelling was required for this 'domain' to select variables for the final model.

3.3 | Clinical predictors

Higher pain at baseline predicted higher pain levels at 3 and 6 months, but a reduction in pain from baseline at 3 months. With respect to disability, higher baseline levels predicted higher pain at 9 months, but not the change in pain at any time point. Neither pain nor disability at baseline predicted 12-month outcomes. No variable in this domain moved forward to the final multivariable models (Tables 2–5).

For measures made at 3 months, both pain and disability predicted higher and increased pain from baseline at every follow-up time point. However, when both factors were included in the *clinical* multivariable models, only pain remained a significant predictor (Tables 6 and 7). Although pain and disability at baseline only accounted for up to 6% of the variance in each of pain level and pain change at follow-ups, pain at 3 months accounted for 39 to 62% of the variance, respectively, at all subsequent follow-up times.

3.4 | History/treatment predictors

Use of healthcare (for LBP; 2.3% used physician, 8.3% physiotherapy, 2.3% chiropractic, 0.5% osteopathic and 5.3% massage services) at baseline predicted reduced pain at 3, 6 and 9 months (Tables 2–5). For measures made at 3 months, use of pain medication (for LBP: 6.0% used analgesic, 4.5% anti-inflammatory and 1.5% muscle relaxant medications) predicted higher pain and increased pain from baseline at every subsequent follow-up time point (Tables 6 and 7). As no other history/treatment factors at baseline (only use of health care) and 3 months (use of pain medication) predicted either outcome at any follow-up time point, these factors progressed to the final multivariable model.

3.5 | Psychological predictors

Higher depressive symptoms (CES-D) at baseline predicted higher pain at 3, 6 and 12 months, and increased pain at each follow-up time point. Higher pain catastrophizing (PCS) predicted higher pain at every follow-up time point, and increased pain at 3 and 6 months, but not thereafter. Higher fear avoidance (work and physical activity related) predicted higher pain, but only at 9 months. After adjustment for the inter-correlation between retained factors in the *psychological* domain models, results differed with respect to outcome. Only depressive symptoms remained predictive of an increase in pain (at every follow-up time point). Both depressive symptoms and pain catastrophizing, and both pain catastrophizing and fear avoidance (work-related only), remained predictors of pain at 3 and 9 months, respectively, but none remained predictive of 12-month pain (Tables 2–5).

For measures made at 3 months, most factors within the psychological domain predicted higher pain and increased pain from baseline (although interpreted oppositely for pain self-efficacy, as lower scores reflect a lower confidence in the ability to do things despite pain) at each follow-up time point. Only a subset of these factors remained significantly predictive after their inclusion in

TABLE 1 Comparison of baseline characteristics between participants that did (FU) and did not (NFU) provide follow-up data at 3, 6, 9 and 12 months

	3 months			6 months	
	Summary statistics			Summary statistics	
Characteristic	**FU (*N* = 120)**	**NFU (*N* = 13)**	***P*-value**	**FU (*N* = 97)**	**NFU (*N* = 36)**
Age (yrs)[†]	29.0 (27.6–30.4)	25.9 (21.2–30.7)	0.187	29.3 (27.7–30.9)	27.1 (24.4–29.7)
Sex (female, %)	50.8	61.5	0.463	48.5	61.1
Body mass index (kg/m^2)[†]	24.3 (23.6–25.1)	24.3 (21.6–27.1)	0.988	24.3 (23.5–25.1)	24.4 (23.1–25.7)
Prev./cur. smoker (yes, %)	36.7	33.3	0.819	37.1	34.3
Marital status (not married/not cohabitating, %)	63.3	66.7	0.819	64.9	60.0
Edu. level (secondary school/ below, %)	25.0	25.0	1.000	24.7	25.7
Empl. status (unemployed, %)	23.3	16.7	0.599	23.7	20.0
Impending comp. (yes, %)	8.3	18.2	0.288	6.4	17.2
Pain (NRS)[†]	5.0 (4.7–5.3)	5.2 (4.1–6.2)	0.790	4.8 (4.4–5.2)	5.6 (5.0–6.1)
Disability (RMDQ)[†]	6.8 (6.0–7.6)	7.9 (4.2–11.6)	0.420	6.5 (5.6–7.3)	8.2 (6.3–10.0)
Previous LBP (yes, %)	94.2	69.2	**0.002**	92.8	88.9
Health care use (yes, %)	18.3	33.3	0.213	18.6	22.9
Pain med. use (yes, %)	20.8	36.4	0.242	19.2	31.0
Depressive sym. (CES-D)[†]	13.4 (11.8–14.9)	21.2 (13.5–28.8)	**0.005**	12.9 (11.2–14.7)	17.2 (13.9–20.5)
Pain catastrophizing (PCS)[†]	13.4 (11.6–15.2)	16.3 (8.8–23.9)	0.348	12.6 (10.7–14.4)	16.8 (12.7–20.9)
Fear avoid.-work (FABQ-W)[†]	11.8 (10.1–13.4)	13.8 (4.3–23.2)	0.501	11.1 (9.3–12.9)	14.3 (10.4–18.1)
Fear avoid.-activity (FABQ-PA)[†]	15.0 (14.0–16.0)	12.0 (9.5–14.5)	0.070	14.8 (13.7–15.9)	14.7 (12.7–16.7)
Pain self-efficacy (PSEQ)[†]	44.8 (42.6–46.9)	37.5 (29.8–45.1)	**0.032**	45.5 (43.2–47.8)	39.9 (35.7–44.1)

Note: Summary statistics (mean [95% CI][†] or percentage [%]) for baseline factors (characteristics) compared between low back pain (LBP) participants who did (follow-up – FU) and did not (non-follow-up – NFU) provide follow-up data, separately at 3, 6, 9 and 12 month time-points using *t* tests (continuous data) or Chi squared tests (categorical data). Significant values are in bold.

Prev./cur., previous/current; edu. level, education level; empl. status, employment status; impending comp., impending compensation; NRS, numerical rating scale; RMDQ, Roland Morris Disability Questionnaire; LBP, low back pain; pain med. use, pain medication use; depressive sym., depressive symptoms; CES-D, Center for Epidemiological Studies Depression Scale; PCS, Pain Catastrophizing Scale; fear avoid-work, fear avoidance related to work; fear avoid-activity, fear avoidance related to physical activity; FABQ, Fear Avoidance Beliefs Questionnaire; PSEQ, Pain Self-Efficacy Questionnaire.

the *psychological* multivariable models: lower pain self-efficacy and higher pain catastrophizing predicted 6- and 9-month pain; lower pain self-efficacy alone predicted 12-month pain; higher fear avoidance (activity related) alone predicted increased pain at 6 months; lower pain self-efficacy and higher depressive symptoms predicted increased pain at 12 months (Tables 6 and 7). Psychological predictors at 3 months accounted for more of the variance in outcome (22–30%) than at baseline (8–20%).

3.6 | Final multivariable models

In the final multivariable models, the factors that remained significant in each domain model were combined. For measures made at baseline, the final models showed that health care usage predicted lower and reduced pain at 3, 6 and 9 months. Similarly, but oppositely, depressive symptoms predicted higher pain at 3 months, and an increase in pain at every follow-up assessment. Other factors at baseline that predicted outcome, albeit for few follow-up time points, included: BMI, sex, impending compensation, pain level and pain catastrophizing. The models accounted for 24% and 26% of the variance in pain and pain change, respectively, at 3 months, reducing to 11% and 14% at 12 months (Tables 2–5).

For measures made at 3 months, only higher pain remained a significant predictor of both higher and increased pain at 6 and 9 months. Outcomes at 12 months were predicted by sex (female – higher pain) and depressive symptoms (increased pain). The models accounted for 62% and 52% of the variance in pain and pain change, respectively, at 6 months, reducing to 55% and 48% at 12 months (Tables 6 and 7).

	9 months			12 months		
	Summary statistics			Summary statistics		
P-value	FU (*N* = 85)	NFU (*N* = 48)	*P*-value	FU (*N* = 94)	NFU (*N* = 39)	*P*-value
0.148	29.3 (27.6–31.0)	27.6 (25.3–30.0)	0.245	29.4 (27.8–31.1)	26.8 (24.5–29.2)	0.084
0.194	48.2	58.3	0.263	51.1	53.8	0.770
0.882	24.4 (23.5–23)	24.3 (23.2–25.3)	0.863	24.2 (23.4–25.1)	24.6 (23.4–25.8)	0.607
0.766	37.6	34.0	0.680	37.2	34.2	0.744
0.602	64.7	61.7	0.731	64.9	60.5	0.637
0.909	23.5	27.7	0.600	25.5	23.7	0.824
0.653	25.9	17.0	0245	21.3	26.3	0.532
0.087	7.5	12.5	0.386	6.8	14.7	0.194
0.044	4.9 (4.5–5.3)	5.2 (4.7–5.8)	0.389	4.9 (4.5–5.3)	5.3 (4.7–5.9)	0.216
0.062	6.3 (5.5–7.2)	8.0 (6.3–9.6)	0.055	6.3 (5.5–7.1)	8.4 (6.5–10.3)	**0.012**
0.469	91.8	91.7	0.984	92.6	89.7	0.592
0.583	21.2	17.0	0.565	20.2	18.4	0.815
0.193	20.9	25.0	0.622	19.2	29.4	0.237
0.018	12.8 (11.0–14.7)	16.3 (13.5–19.1)	**0.036**	12.9 (11.1–14.7)	17.0 (13.7–20.3)	**0.021**
0.035	12.4 (10.5–14.4)	15.9 (12.5–19.3)	0.059	12.3 (10.4–14.1)	17.2 (13.3–21.1)	**0.012**
0.099	11.0 (9.2–2.7)	13.7 (10.3–17.2)	0.113	11.6 (9.8–13.4)	12.8 (9.0–16.7)	0.516
0.944	14.7 (13.6–15.9)	14.8 (13.1–16.5)	0.919	14.9 (13.8–16.0)	14.3 (12.4–16.2)	0.549
0.015	46.2 (43.8–48.6)	40.3 (36.7–44.0)	**0.006**	45.9 (43.5–48.3)	40.0 (36.2–43.7)	**0.007**

4 | DISCUSSION

This study is the first to attempt to consider the impact of time variation of candidate risk factors on long-term outcome from the very early-onset of acute LBP. The results confirm that many risk factors differ over time. With respect to the first aim, we showed that at baseline (i.e., acute phase) higher depressive symptoms most consistently predicted worse outcomes over the 12-month period. Conversely, more health care usage predicted lower and reduced pain at 3, 6 and 9 months. Several other factors at baseline (e.g., BMI, sex, impending compensation and pain level) also predicted outcome, albeit inconsistently across time points. With respect to our second aim, we showed that at 3 months psychological factors in general were more predictive of outcome than when measured at baseline, and greater pain medication usage predicted worse outcomes at every subsequent follow-up time point. However, higher pain at 3 months more strongly and consistently predicted poor outcome than any other factor. Moreover, a greater proportion of variance in long-term outcome was accounted for by factors measured at 3 months than at baseline. The findings may have important implications for the clinical management of LBP.

4.1 | Risk factors differ depending on when they are measured

Predictors identified from measures made in the acute phase of LBP corroborate other data of early psychosocial predictors of LBP chronicity. At baseline (early-acute), depressive symptoms consistently predicted

TABLE 2 Linear regression models relating the *change in pain* from baseline to 3 and 6 months with baseline factors

Factor at baseline	3 months (% change in pain from baseline)						6 months (% change in pain from baseline)					
	Unadjusted		Domain adjusted		Final Model		Unadjusted		Domain adjusted		Final Model	
	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2
Sociodemographic						**0.26*****						**0.15*****
Age (yrs)	−0.01 (0.00)	0.02		**0.06****			−0.01 (0.01)	0.02				
Sex (female)	0.10 (0.07)	0.02					0.01 (0.08)	0.00				
BMI (kg/m^2)	**−0.02 (0.01)****	**0.06****	**−0.02 (0.01)****		**−0.02 (0.01)***		−0.01 (0.01)	0.02				
Prev./cur. smoker	0.09 (0.07)	0.01					0.15 (0.09)	0.03				
Marital status	0.07 (0.07)	0.01					0.13 (0.09)	0.02				
Edu. level	0.12 (0.08)	0.02					0.03 (0.10)	0.00				
Empl. status	0.04 (0.08)	0.00					0.06 (0.10)	0.00				
Impending comp.	−0.02 (0.15)	0.00					0.10 (0.18)	0.00				
Clinical												
Pain (NRS)	**−0.05 (0.02)***	**0.05***	**−0.05 (0.02)***	**0.05***	**−0.04 (0.02)****		−0.02 (0.02)	0.01				
Disability (RMDQ)	−0.00 (0.01)	0.00)					−0.01 (0.01)	0.01				
History/treatment												
Previous LBP	0.15 (0.15)	0.01		**0.04***			0.26 (0.16)	0.03		**0.06***		
Health care use	**−0.20 (0.09)***	**0.04***	**−0.20 (0.09)***		**−0.17 (0.08)***		**−0.26 (0.10)***	**0.06***	**−0.26 (0.10)***		**−0.26 (0.10)***	
Pain med. use	−0.07 (0.10)	0.01					−0.16 (0.11)	0.03				
Psychological												
Depressive sym.	**0.02 (0.00)*****	**0.13*****	**0.01 (0.00)****	**0.15*****	**0.02 (0.00)*****		**0.01 (0.00)****	**0.09****	**0.01 (0.00)***	**0.12****	**0.01 (0.00)****	
Pain catastrophizing	**0.01 (0.00)****	**0.06****	0.00 (0.00)				**0.01 (0.00)***	**0.06***	0.01 (0.00)			
Fear avoid.-work	−0.00 (0.00)	0.00					0.01 (0.00)	0.01				
Fear avoid.-activity	−0.00 (0.01)	0.00					0.00 (0.01)	0.00				
Pain self-efficacy	−0.00 (0.00)	0.00					−0.00 (0.00)	0.00				

Note: Yrs, years; BMI, body mass index; Prev/cur. smoker, previous or current smoker; edu level, education level; empl. status, employment status; impending comp., impending compensation; NRS, numerical rating scale; RMDQ, Roland Morris Disability Questionnaire; LBP, low back pain; pain med. use, pain medication use; depressive sym., depressive symptoms; fear avoid-work, fear avoidance related to work; fear avoid-activity, fear avoidance related to physical activity.

$^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$.

TABLE 3 Linear regression models relating the *change in pain* from baseline to 9 and 12 months with baseline factors.

Factor at baseline	9 months (% change in pain from baseline)						12 months (% change in pain from baseline)					
	Unadjusted		Domain adjusted		Final Model		Unadjusted		Domain adjusted		Final Model	
	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2
Sociodemographic						**0.15****						**0.14****
Age (yrs)	−0.00 (0.01)	0.01					0.00 (0.01)	0.00		0.09		
Sex (female)	0.10 (0.09)	0.02					**0.18 (0.08)***	**0.05***	0.15 (0.08)			
BMI (kg/m^2)	−0.00 (0.01)	0.00					**−0.02 (0.01)***	**0.06***	**−0.02 (0.01)***		**−0.02 (0.01)***	
Prev./cur. smoker	0.08 (0.09)	0.01					0.03 (0.09)	0.00				
Marital status	−0.01 (0.09)	0.00					−0.04 (0.09)	0.00				
Edu. level	−0.01 (0.11)	0.00					0.06 (0.10)	0.00				
Empl. status	0.07 (0.10)	0.01					−0.06 (0.10)	0.00				
Impending comp.	0.17 (0.18)	0.01					0.08 (0.19)	0.00				
Clinical												
Pain (NRS)	−0.04 (0.02)	0.03										
Disability (RMDQ)	0.02 (0.01)	0.03										
History/treatment												
Previous LBP	0.28 (0.16)	0.04		**0.06***			0.22 (0.16)	0.02				
Health care use	**−0.25 (0.11)***	**0.06***	**−0.25 (0.11)***		**−0.26 (0.10)***		−0.17 (0.10)	0.03				
Pain med. use	−0.06 (0.12)	0.00					−0.13 (0.12)	0.02				
Psychological												
Depressive sym.	**0.01 (0.00)****	**0.08****	**0.01 (0.00)****	**0.08****	**0.01 (0.00)****		**0.01 (0.00)****	**0.09****	**0.01 (0.00)****	**0.09****	**0.01 (0.00)****	
Pain catastrophizing	0.01 (0.00)	0.04					0.00 (0.00)	0.01				
Fear avoid.-work	0.01 (0.01)	0.04					0.01 (0.00)	0.02				
Fear avoid.-activity	0.01 (0.01)	0.03					−0.00 (0.01)	0.00				
Pain self-efficacy	−0.00 (0.00)	0.01					−0.00 (0.00)	0.02				

Note: Refer to Tables 1 and 2 for abbreviations.

$^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$.

TABLE 4 Linear regression models relating *pain level* at 3 and 6 months with baseline factors

Factor at baseline	3 months (pain level)						6 months (pain level)					
	Unadjusted			Domain adjusted	Final Model			Unadjusted	Domain adjusted		Final Model	
	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2
Sociodemographic						**0.24*****						**0.14*****
Age (yrs)	−0.04 (0.02)	0.02		**0.07**			−0.04 (0.03)	0.02				
Sex (female)	0.54 (0.38)	0.02					−0.05 (0.44)	0.00				
BMI (kg/m^2)	**−0.14 (0.05)****	**0.07**	**−0.14 (0.05)****		**−0.10 (0.04)***		−0.07 (0.05)	0.02				
Prev./cur. smoker	0.46 (0.39)	0.01					0.81 (0.45)	0.03				
Marital status	0.51 (0.39)	0.01					0.66 (0.46)	0.02				
Edu. level	0.29 (0.44)	0.00					0.11 (0.51)	0.00				
Empl. status	0.25 (0.45)	0.00					0.29 (0.52)	0.00				
Impending comp.	0.88 (0.79)	0.01					*1.84 (0.96)*$^{\Delta}$	*0.05*$^{\Delta}$				
Clinical												
Pain (NRS)	**0.23 (0.10)***	**0.04***	**0.23 (0.10)***	**0.04***	0.18 (0.09)		**0.26 (0.11)***	**0.06***	**0.26 (0.11)***	**0.06***	0.16 (0.11)	
Disability (RMDQ)	0.01 (0.04)	0.00					−0.02 (0.05)	0.00				
History/treatment												
Previous LBP	0.70 (0.81)	0.01					1.11 (0.84)	0.02				
Health care use	−0.71 (0.49)	0.02					−1.01 (0.56)	0.03				
Pain med. use	−0.26 (0.54)	0.00					−0.30 (0.61)	0.00				
Psychological												
Depressive sym.	**0.09 (0.02)*****	**0.14*****	**0.07 (0.02)****	**0.18*****	**0.07 (0.02)****		**0.07 (0.02)****	**0.08****	0.05 (0.02)	**0.15*****		
Pain catastrophizing	**0.07 (0.02)*****	**0.11*****	**0.05 (0.02)***		0.03 (0.02)		**0.08 (0.02)*****	**0.12*****	**0.07 (0.02)****		**0.07 (0.02)****	
Fear avoid.-work	−0.00 (0.02)	0.00					0.02 (0.02)	0.00				
Fear avoid.-activity	−0.01 (0.03)	0.00					0.03 (0.04)	0.01				
Pain self-efficacy	−0.02 (0.02)	0.01					−0.02 (0.02)	0.01				

Note: Refer to Tables 1 and 2 for abbreviations.

$\Delta p = 0.060$

$^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$.

TABLE 5 Linear regression models relating *pain level* at 9 and 12 months with baseline factors

Factor at baseline	9 months (pain level)						12 months (pain level)					
	Unadjusted		Domain adjusted		Final Model		Unadjusted		Domain adjusted		Final Model	
	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2
Sociodemographic						**0.18****						**0.11****
Age (yrs)	−0.02 (0.03)	0.00		**0.12****			0.03 (0.03)	0.02		**0.11****		
Sex (female)	0.46 (0.44)	0.01					**1.07 (0.43)***	**0.06***	**0.91 (0.43)***		**0.91 (0.43)***	
BMI (kg/m^2)	−0.03 (0.05)	0.00					**−0.13 (0.05)***	**0.07***	**−0.11 (0.05)***		**−0.11 (0.05)***	
Prev./cur. smoker	0.44 (0.46)	0.01					0.15 (0.46)	0.00				
Marital status	−0.26 (0.46)	0.00					−0.28 (0.47)	0.00				
Edu. level	−0.38 (0.52)	0.01					−0.08 (0.51)	0.00				
Empl. status	0.43 (0.51)	0.01					−0.35 (0.55)	0.00				
Impending comp.	**2.65 (0.90)****	**0.12****	**2.65 (0.90)****		**2.20 (0.92)***		1.36 (1.01)	0.02				
Clinical												
Pain (NRS)	0.19 (0.12)	0.03		**0.06***			*0.22 (0.12)*$^{\#}$	*0.04*$^{\Delta}$				
Disability (RMDQ)	**0.13 (0.05)***	**0.06***	**0.13 (0.05)***		0.06 (0.06)		0.03 (0.06)	0.00				
History/treatment												
Previous LBP	1.25 (0.80)	0.03					1.00 (0.85)	0.01				
Health care use	−0.82 (0.54)	0.03					−0.49 (0.56)	0.01				
Pain med. use	−0.18 (0.62)	0.00					−0.40 (0.66)	0.01				
Psychological												
Depressive sym.	*0.05 (0.03)*$^{\Delta}$	*0.04*$^{\Delta}$		**0.20*****			**0.06 (0.03)***	**0.06***	*0.05 (0.03)*$^{\Delta}$	**0.08***		
Pain catastrophizing	**0.07 (0.02)****	**0.11****	**0.06 (0.02)***		0.03 (0.03)		**0.05 (0.02)***	**0.05***	0.04 (0.02)			
Fear avoid.-work	**0.07 (0.03)***	**0.08***	**0.05 (0.03)***		0.04 (0.03)		0.03 (0.03)	0.01				
Fear avoid.-activity	**0.10 (0.04)***	**0.07***	0.07 (0.04)				0.01 (0.04)	0.00				
Pain self-efficacy	−0.05 (0.02)	0.05					*−0.05 (0.02)*$^{\Delta}$	*0.05*$^{\Delta}$				

Note: Refer to Tables 1 and 2 for abbreviations.

$\Delta p < 0.067$

$^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$.

TABLE 6 Linear regression models relating the *change in pain* from baseline to 6, 9 and 12 months with factors at 3 months

Factor at 3 months	6 months (% change in pain from baseline)						9 months (% change in pain from baseline)	
	Unadjusted		Domain adjusted		Final Model		Unadjusted	
	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2
Sociodemographic						**0.52*****		
Age (yrs)	−0.01 (0.01)	0.02					−0.00 (0.01)	0.01
Sex (female)	0.01 (0.08)	0.00					0.10 (0.09)	0.02
BMI (kg/m^2)	−0.02 (0.01)	0.03					−0.01 (0.01)	0.00
Prev./cur. smoker	0.10 (0.09)	0.01					0.05 (0.09)	0.00
Marital status	−0.03 (0.03)	0.02					−0.04 (0.09)	0.00
Edu. level	0.04 (0.11)	0.00					0.06 (0.11)	0.00
Empl. status	−0.05 (0.11)	0.00					0.02 (0.11)	0.00
Impending comp.	0.10 (0.21)	0.00					0.12 (0.21)	0.00
Clinical								
Pain (NRS)	**0.15 (0.02)*****	**0.49*****	**0.14 (0.02)*****	**0.50*****	**0.13 (0.02)*****		**0.13 (0.02)*** **	**0.42*****
Disability (RMDQ)	**0.04 (0.01)*****	**0.15*****	0.01 (0.1)				**0.04 (0.01)*** **	**0.16*****
History/treatment								
Previous LBP	0.26 (0.16)	0.03		**0.08***			0.28 (0.16)	0.04
Health care use	0.02 (0.10)	0.00					0.04 (0.10)	0.00
Pain med. use	**0.31 (0.12)***	**0.08***	**0.31 (0.12)***		0.09 (0.09)		**0.28 (0.12)***	**0.07***
Psychological								
Depressive sym.	**0.01 (0.00)***	**0.05***	0.00 (0.00)	**0.25*****			**0.01 (0.00)***	**0.06***
Pain catastrophizing	**0.02 (0.01)****	**0.10****	0.00 (0.01)				**0.02 (0.00)****	**0.09****
Fear avoid.-work	**0.02 (0.00)*****	**0.13**	**0.01 (0.00)***		*0.01 (0.00)*$^{\Delta}$		**0.02 (0.00)****	**0.12****
Fear avoid.-activity	0.01 (0.01)	0.03					0.00 (0.01)	0.00
Pain self-efficacy	**−0.01 (0.00)*****	**0.18*****	**−0.01 (0.00)***		0.00 (0.00)		**−0.01 (0.00)****	**0.14****

Note: Refer to Tables 1 and 2 for abbreviations.

$\Delta p = 0.057$

$^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$.

poorer outcome. Burns et al. (Burns et al., 2020) similarly showed that people presenting to emergency with an acute LBP complaint had a delayed or failed recovery (by 3 months) if they also experienced depressive symptoms. We also found that baseline measure of pain catastrophizing predicted pain up to 9 months later, and co-prediction with depressive symptoms at some time points. Additive effects of early pain catastrophizing and depressed mood on outcome have been reported (Bergbom et al., 2011; Linton et al., 2011). These findings highlight the value of consideration of both depressive symptoms and pain catastrophizing in the first few weeks after LBP onset.

Depressive symptoms measured at 3 months less consistently predicted outcome than measures made at baseline. This concurs with data that worse disability at 1-year follow-up was more strongly predicted for those with higher depressive symptoms in acute (≤3 weeks) than chronic (>3, but <52 weeks) LBP (Burton et al., 1995). Depressive symptoms might be a more influential determinant of outcome during the early-acute phase regardless of the later trajectory of depressed mood. A possible causal pathway between early depressive mood and poor outcome might be explained by underlying inflammatory processes. Inflammation is involved in the exacerbation and pathophysiology of depression (Fasick et al., 2015; Felger & Lotrich, 2013; Kaster et al., 2012; Tuglu et al., 2003), and depression can enhance inflammation (Fasick et al., 2015; Kubera et al., 2011). Using the same cohort as the present analysis, we showed recently that individuals with the worst recovery had both higher depressive symptoms and a unique pro-inflammatory profile during early-acute LBP (Klyne et al., 2021a; Klyne, Barbe, et al., 2018). As inflammation and depression can fuel each other in a bidirectional manner (Beurel et al., 2020), a disturbance to either, such as the onset of LBP, could

				12 months (% change in pain from baseline)					
Domain adjusted		**Final Model**		**Unadjusted**		**Domain adjusted**		**Final Model**	
Coe. (SE)	R^2	**Coe. (SE)**	R^2	**Coe. (SE)**	R^2	**Coe. (SE)**	R^2	**Coe. (SE)**	R^2
			0.43***						**0.48*****
				0.00 (0.01)	0.00		**0.05***		
				0.18 (0.08)*	**0.05***	**0.18 (0.08)***		0.11 (0.07)	
				−0.02 (0.01)	0.04				
				−0.01 (0.09)	0.00				
				−0.03 (0.09)	0.00				
				0.08 (0.11)	0.01				
				−0.03 (0.12)	0.00				
				−0.06 (0.24)	0.00				
0.12 (0.02)***	**0.43*****	**0.12 (0.02)*****		**0.13 (0.02)*****	**0.39*****	**0.13 (0.02)*****	**0.39*****	**0.10 (0.02)*****	
0.01 (0.01)				**0.03 (0.01)****	**0.10****	0.00 (0.01)			
	0.07*			0.22 (0.16)	0.02		**0.08***		
				0.04 (0.10)	0.00				
0.28 (0.12)*		0.09 (0.10)		**0.30 (0.12)***	**0.08***	**0.30 (0.12)***		0.07 (0.10)	
0.00 (0.00)	**0.22****			**0.01 (0.00)****	**0.10****	**0.01 (0.00)***	**0.30*****	**0.01 (0.00)***	
0.01 (0.01)				**0.01 (0.01)***	**0.07***	−0.00 (0.01)			
0.01 (0.01)				**0.02 (0.00)****	**0.10****	0.01 (0.01)			
				0.00 (0.01)	0.00				
−0.01 (0.00)				**−0.02 (0.00)*****	**0.22*****	**−0.01 (0.00)****		−0.00 (0.00)	

setup a negative cycle between the two that mediates LBP persistence.

Our univariate models showed that a broader range of psychological factors predicted outcome, with a greater percentage of variance explained, when measured at 3 months than at baseline. This concurs with evidence from systematic reviews that psychological factors (including fear avoidance/coping strategies) in early LBP do not predict chronicity (Pincus et al., 1976, 2006), whereas studies of individuals with more persistent LBP have high prevalence of concordant psychological factors (Dersh et al., 1976; Hagen et al., 1976; Strine & Hootman, 2007), of which many are associated with long-term outcome (Burton et al., 2004; Grotle et al., 2006, 2010; Henschke et al., 2008). The difference in risk associated with earlier or later presentation of these features might be explained by the adaptive and protective nature of certain emotional responses to acute pain, which might become maladaptive when pain persists. For instance, fear of pain and diminished self-efficacy seem to have a role only in the later stages of LBP, in which a negative cycle of cognition-emotion-behaviour is already established – with depression as a potential early trigger (Pincus et al., 2006). Each specific psychological factor appears to contribute differently depending on the stage of LBP and this might explain why reviews (e.gFoster et al., 2010; Ramond-Roquin et al., 2015)) that include people with LBP of mixed duration (e.g., acute, sub-acute, sub-chronic) generally fail to identify reliable psychological predictors of chronicity. Pinpointing the stage of LBP, or context, under which specific psychological features begin to contribute or maximally contribute to outcome is an important area of future research.

TABLE 7 Linear regression models relating *pain level* at 6, 9 and 12 months with factors at 3 months

Factor at 3 months	6 months (pain level)						9 months (pain level)	
	Unadjusted		Domain adjusted		Final Model		Unadjusted	
	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2
Sociodemographic						**0.62*****		
Age (yrs)	−0.04 (0.03)	0.02					−0.02 (0.03)	0.00
Sex (female)	−0.05 (0.44)	0.00					0.46 (0.44)	0.01
BMI (kg/m^2)	−0.09 (0.05)	0.03					−0.04 (0.05)	0.01
Prev./cur. smoker	0.44 (0.46)	0.01					0.24 (0.46)	0.00
Marital status	0.32 (0.46)	0.01					−0.30 (0.46)	0.01
Edu. level	0.28 (0.56)	0.00					−0.04 (0.57)	0.00
Empl. status	0.42 (0.58)	0.01					0.62 (0.56)	0.01
Impending comp.	1.31 (1.12)	0.02					**2.23 (1.05)***	**0.06***
Clinical								
Pain (NRS)	**0.86 (0.07)*****	**0.62*****	**0.86 (0.08)*****	**0.62*****	**0.82 (0.10)*****		**0.74 (0.07)*****	**0.55*****
Disability (RMDQ)	**0.22 (0.05)*****	**0.15*****	−0.00 (0.04)				**0.23 (0.05)*****	**0.19*****
History/treatment								
Previous LBP	1.11 (0.84)	0.02		**0.11****			1.25 (0.80)	0.03
Health care use	0.12 (0.52)	0.00					0.48 (0.50)	0.01
Pain med. use	**1.94 (0.61)****	**0.11****	**1.94 (0.61)****		0.66 (0.44)		**1.48 (0.64)***	**0.07***
Psychological								
Depressive sym.	0.03 (0.02)	0.02		**0.24*****			0.02 (0.02)	0.01
Pain catastrophizing	**0.11 (0.03)*****	**0.18*****	**0.07 (0.03)***		0.00 (0.02)		**0.11 (0.02)*****	**0.21*****
Fear avoid.-work	**0.06 (0.02)***	**0.06***	0.02 (0.03)				**0.08 (0.02)****	**0.11****
Fear avoid.-activity	0.06 (0.03)	0.03					0.04 (0.03)	0.02
Pain self-efficacy	**−0.08 (0.02)*****	**0.19*****	**−0.05 (1.28)****		0.01 (0.02)		**−0.01 (0.02)*****	**0.20*****

Note: Refer to Tables 1 and 2 for abbreviations.

$^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$.

4.2 | Early use of healthcare but later use of pain medication oppositely predict outcome

A finding that appears to contrast recommendations from current clinical practice guidelines was that participants who sought health care – which involved physiotherapy and/or massage ~75% of the time – during acute LBP were more likely to experience reduced pain by 3, 6 and 9 months. Current clinical guidelines recommend minimal early intervention, especially in the first few weeks (de Campos, 2017; Qaseem et al., 2017; Stochkendahl et al., 2018; Van Wambeke et al., 2017). Although our data do not distinguish between treatment in the first 6 weeks (which would be incongruent with current guidelines) from treatment between 6 weeks and 3 months (which is not discouraged), the findings suggest that recommendations regarding early intervention might require reconsideration.

In contrast, individuals who used pain medication at 3 months had elevated risk of greater pain and an increase in pain at subsequent follow ups. There are at least two plausible and perhaps overlapping explanations for this. First, the participants who used medications by 3 months might be those with worse symptoms, and thus more likely to continue to experience poor recovery. Second, the long-term efficacy of analgesics and anti-inflammatories, which were the medication of choice ~90% of the time in this study, is generally poor or unclear at best (Foster et al., 2009; Gregori et al., 2018; Trescot et al., 2008). For example, paracetamol (most widely used analgesic) is considered no better than placebo for non-specific LBP (Saragiotto et al., 2016), non-steroidal anti-inflammatory drugs have small effect sizes (Machado et al., 2017) and can be counterproductive when introduced at certain stages post-injury (Stovitz & Johnson, 2003; Ziltener et al., 2010), and opioids are

				12 months (pain level)					
Domain adjusted			Final Model	Unadjusted		Domain adjusted		Final Model	
Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2	Coe. (SE)	R^2
			0.55***						**0.55*****
	0.06*			0.03 (0.03)	0.01		**0.06***		
				1.07 (0.43)*	**0.06***	**1.07 (0.43)***		**0.71 (0.36)***	
				−0.10 (0.05)	0.04				
				−0.21 (0.48)	0.00				
				−0.25 (0.48)	0.00				
				0.29 (0.56)	0.00				
				0.05 (0.50)	0.00				
2.23 (1.05)*		0.64 (0.79)		0.27 (1.28)	0.00				
0.70 (0.09)***	**0.55*****	**0.65 (0.11)*****		**0.75 (0.08)*****	**0.47*****	**0.74 (0.09)*****	**0.47*****	**0.60 (0.10)*****	
0.05 (0.04)				**0.19 (0.06)*****	**0.11*****	0.00 (0.05)			
	0.07*			1.00 (0.85)	0.01		**0.11****		
				0.41 (0.52)	0.01				
1.48 (0.64)*		0.43 (0.49)		**1.88 (0.63)****	**0.11****	**1.88 (0.63)****		0.59 (0.49)	
	0.30***			0.04 (0.02)	0.03		**0.28*****		
0.08 (0.03)*		0.02 (0.02)		**0.10 (0.03)*****	**0.14*****	0.04 (0.03)			
0.03 (0.03)				**0.06 (0.03)***	**0.06***	0.02 (0.03)			
−0.03 (0.03)				0.04 (0.03)	0.02				
−0.05 (0.02)*		−0.00 (0.02)		**−0.09 (0.02)*****	**0.25*****	**−0.07 (0.02)****		−0.02 (0.02)	

increasingly viewed as an inappropriate treatment for long-term pain as they become less effective and come with considerable side effects. There is also compelling evidence that opioid use for as brief a period of 1 month increases the risk of developing depression (Scherrer et al., 2016), which is a risk factor for persistent LBP as shown in this and other studies (Pinheiro et al., 2016). Whether individuals in the current cohort who used medication were more likely to continue to use medication, and whether this resulted in worse outcomes would be important to consider.

4.3 | Other predictors of outcome

As expected, intensity of pain at baseline and 3 months predicted future pain. However, the strength and consistency of this relationship depended on the time point during the trajectory of LBP. Higher baseline pain levels were predictive of higher short-term pain (3, 6 months), yet a reduction in pain (from baseline) at 3 months. The latter was anticipated because pain is often most severe during the early-acute phase, and individuals with higher levels have more potential for change. On the other hand, pain levels recorded at 3-months (higher) strongly predicted higher pain and an increase in pain at every follow-up time point over the 12 months. This suggests that pain that recurs or persists (chronic) for up to 3 months is a more reliable prognostic factor of outcome in the later stages of LBP. That pain during the early-acute phase weakly and unreliably predicted outcome has also been shown previously in this cohort (Klyne et al., 2018, 2019).

Being female, having a lower BMI or having LBP-related impending compensation were associated with worse outcome at some time points. The association between being female and both higher pain and an increase in pain at

12 months concurs with other data that females report higher prevalence are more severely affected and have a worse prognosis of LBP, and pain more generally, than men (Fillingim et al., 2003; Leveille et al., 2005). Multiple biological and psychological factors are likely to explain these gender differences, with emerging evidence for the role of oestrogens (Mogil, 2012), pain-related genes and maladaptive coping strategies (Bartley & Fillingim, 2013), among others.

The association between lower BMI at baseline and poorer outcomes at 3 and 12 months appears to contradict evidence linking obesity to the prevalence (Shiri et al., 2010) and causation (Chou et al., 2016; Samartzis et al., 2013; Wilkins et al., 2018) of LBP. This might be explained by the inclusion of few overweight/obese (BMI ≥30 kg/m^2, N=8) participants, and that underweight, like overweight, is associated with numerous comorbidities such as depression (Jung et al., 2017). The association between impending compensation (baseline, 3 months) and greater 9-month pain concurs with other data (Harris et al., 2005; Hayden et al., 2009; Pincus et al., 2008).

Although a prior history of LBP is generally considered a predictor of poor outcome (Papageorgiou et al., 1996), this variable was not retained in our models. This is probably explained by the very small proportion of individuals who reported no history of LBP (~8%), and is consistent with research that is beginning to show that for most, LBP is an ongoing condition marked by periods of flare and remission (Dunn et al., 2013; Kongsted et al., 2015).

4.4 | Clinical implications

These findings have important clinical implications. First, they highlight the need to consider both a diverse range of factors and their potential time variance when assessing risk of poor outcome. Extending from other observations of the relevance of depressive symptoms during the early-acute phase (Klyne, Barbe, et al., 2018; Klyne & Hodges, 2020; Klyne et al., 2019), these data show a strong relationship between a broader range of psychological symptoms and poor outcome when they are assessed at 3 months. This presents a potential argument for evaluating and treating these features during both the early-acute and later phases of LBP. Second, that the early use of healthcare predicted better recovery presents a potential contrary argument to the contemporary guidelines regarding minimal early intervention.

4.5 | Methodological considerations

Several limitations require consideration. First, we managed the large number of candidate predictor factors by first analysing them in their meaningful domain (i.e., sociodemographic, clinical, history/treatment, psychological). Although this approach allowed selection of the key predictor(s) from each domain before moving them onto a final multivariable model, it is possible that factors within one domain could have influenced factors in another domain had they been modelled together. We did not use stepwise regression because this is generally disparaged due to limitations that can generate misleading results (Smith, 2018). Second, other additional uncontrolled factors might have affected the results found, such as genetic factors (Bjorland et al., 2016; Tegeder & Lotsch, 2009), lifestyle factors (including sleep and physical activity habits, diet and alcohol consumption) (Klyne, Barbe, et al., 2018, 2019, Klyne, Barbe, Hodges, 2021, Klyne, Barbe, James, et al., 2021) and environmental factors (e.g., temperature, humidity and pressure) (Beukenhorst et al., 2020), which are associated with LBP. Third, mean scores for many of the psychological measures were mild/in the non-clinical range, which may have limited their impact on outcomes. Fourth, missing data due to attrition may have influenced results. It is potentially important that the group who did not return for follow-up had more significant psychological features. This means that our results may underestimate the impact of these psychological features, but we do not believe that this undermines our main conclusions. Fifth, our findings with respect to medication and healthcare usage did not consider the 'type' or 'frequency' of treatment as the study was not powered to assess these questions. Sixth, we did not aim to categorize individuals based on their underlying pain mechanisms (i.e., nociceptive, nociplastic and neuropathic) as our intention was to determine whether specific factors at different time points post-acute LBP onset predicted outcome, regardless of the initial underlying mechanisms. However, it is important to note that the factors that impact the trajectory of LBP could be very different depending on the underlying mechanisms. Seventh, findings should be interpreted with consideration of the sampling limitations (e.g., age restricted to 50 years old, computer literate and access to the internet) and bias towards recruiting participants affiliated and/or in proximity with the University.

5 | CONCLUSIONS

The results of this study highlight the need to consider both a diverse range of factors and their potential time variance along the trajectory of LBP when assessing risk of poor outcome. Although some factors were prognostic of short-term outcome, some long-term outcome, some

both, and others neither, they weighted differently depending on whether the LBP was acute or had already transitioned to chronicity.

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CONFLICT OF INTERESTS

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AUTHOR CONTRIBUTIONS

DMK contributed to conceptualization of study, study design, data collection, analysis, manuscript preparation and review. PWH contributed to conceptualization of study, study design, analysis, manuscript preparation and review and funding. LMH contributed to data entry and manuscript review. MKN contributed to study design and review and funding. All authors discussed the results and commented on the manuscript.

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