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Framework for improving outcome prediction for acute to chronic low back pain transitions

Steven Z. George[a,*], Trevor A. Lentz[a], Jason M. Beneciuk[b,c], Nrupen A. Bhavsar[d], Jennifer M. Mundt[e], Jeff Boissoneault[f]

Abstract

Clinical practice guidelines and the Federal Pain Research Strategy (United States) have recently highlighted research priorities to lessen the public health impact of low back pain (LBP). It may be necessary to improve existing predictive approaches to meet these research priorities for the transition from acute to chronic LBP. In this article, we first present a mapping review of previous studies investigating this transition and, from the characterization of the mapping review, present a predictive framework that accounts for limitations in the identified studies. Potential advantages of implementing this predictive framework are further considered. These advantages include (1) leveraging routinely collected health care data to improve prediction of the development of chronic LBP and (2) facilitating use of advanced analytical approaches that may improve prediction accuracy. Furthermore, successful implementation of this predictive framework in the electronic health record would allow for widespread testing of accuracy resulting in validated clinical decision aids for predicting chronic LBP development.

Keywords: Chronic pain, Outcome prediction, Pain research

1. Introduction

Chronic pain occurs more frequently than other conditions already widely accepted as public health priorities, with an overall prevalence higher than diabetes, cardiovascular disease, and cancer combined.[45] Exact estimates vary based on case definitions, but the prevalence for chronic pain has been reported to be as high as 110 million people in the United States.[45] The economic impact of chronic pain is accordingly large, with direct and indirect costs totaling $650 billion.[45] In the United States[41,65] and Canada,[24] the ongoing opioid crisis is further evidence of chronic pain's societal impact. Low back pain (LBP) is the largest subset of chronic pain conditions,[45] and rates are increasing. For example, the prevalence of chronic back pain in North Carolina increased from 3.9% in 1992 to 10.2% in 2006.[27] Since 1990, the global prevalence of LBP has increased by 17.3%, and it continues to be a leading cause of global years lived with disability.[34,35]

Accordingly, LBP pain is one of the most common reasons to seek health care.[27,45] Clinical practice guidelines[19,73] and the Federal Pain Research Strategy (United States)[31] highlight priorities for addressing the discord between increasing health care utilization and growing societal impact of LBP.[34,35] Limiting the transition of acute pain to chronic LBP is a top research priority cited in these clinical practice guidelines[19,73] and the Federal Pain Research Strategy (United States).[31] Improving prediction accuracy for transition to chronic LBP is a vital precursor to development effective treatment strategies that limit this transition. For example, the Federal Pain Research Strategy (United States) has highlighted the importance of optimizing screening tools for predicting the development of persistent pain conditions. Implementation of systematic approaches with high predictive accuracy is likely necessary before health care systems can efficiently manage acute LBP by preventing development of chronic LBP conditions.[59]

In this review, we first describe variability in predictors, outcome measures, analytical approaches, and predictive accuracy from previous studies investigating the acute to chronic LBP transition. The variability in these factors were identified by mapping review, which is used to characterize the quantity and quality of a body of literature for the purposes of making recommendations for future research.[38] We then describe a standardized predictive framework for the transition from acute

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[a] Department of Orthopaedic Surgery, Duke Clinical Research Institute, Duke University, Durham, NC, USA, [b] Department of Physical Therapy, University of Florida, Gainesville, FL, USA, [c] Brooks Rehabilitation, University of Florida College of Public Health & Health Professions Research Collaboration, Jacksonville, FL, USA, [d] Division of General Internal Medicine, Duke University, Durham, NC, USA, [e] Department of Neurology, Northwestern University Feinberg School of Medicine, Chicago, IL, USA, [f] Department of Clinical and Health Psychology, University of Florida, Gainesville, FL, USA

**Corresponding author. Address: Department of Orthopaedic Surgery, Duke Clinical Research Institute, Duke University, 200 Morris Street, Durham, NC. Tel.: (919) 668-0825. E-mail address: steven.george@duke.edu (S.Z. George).*

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to chronic LBP that aims to address the variability identified from the mapping review by improving methods for predicting the development of chronic LBP. Application of this predictive framework will be considered with the goal of implementing in real-world settings in mind by leveraging novel data sources, including the electronic health record (EHR), to improve prediction of chronic LBP.

2. Mapping review

In comparison with other review options (eg, scoping or systematic review), mapping reviews search based on time and scope constraints.[38] Therefore, mapping reviews are not meant to offer an exhaustive, comprehensive, and/or definitive review of a topic. Instead, they are used to characterize a body of literature by identifying key study design elements, with the overall goal of providing informed direction for future primary or secondary research.[38] Mapping review results are typically presented in tabular format at the individual study level (ie, no attempt at pooling) and without formal quality assessment.[38] A mapping review was included in this review to provide structure to identifying sources of variability from previous predictive studies of acute to chronic LBP transition. The sources of variability selected to highlight from the mapping review were in areas relevant to developing a predictive framework and included: (1) individual predictors; (2) outcome measures; (3) analytical approach; and (4) prediction accuracy.

2.1. Search strategy and study selection

PubMed and Google Scholar searches were conducted in July 2018 using combinations of the following terms: back pain, LBP, acute to chronic, persistent pain, chronicity, prospective, longitudinal, long-term, prognosis, prognostic, predict, outcome, and transition. Potential articles were then identified by independently screening titles and abstracts. Full articles were evaluated by 2 coauthors (J.M.M. and J.B.), who reached consensus on inclusion through discussion. In cases when consensus could not be reached, a third author (S.Z.G.) provided an independent assessment of the article.

Studies were selected for the mapping review based on the following criteria: (1) study population consisting of individuals with acute or subacute LBP (<3 months), (2) follow-up period of at least 12 months, (3) examined predictors of LBP outcomes (rather than only measuring the likelihood of having certain outcomes), (4) not a clinical trial, and (5) used clinically feasible measures for predictors and outcome (eg, excluding structural/functional MRI studies). We did identify 2 neuroimaging studies that characterized brain-derived markers for predicting chronicity of LBP.[2,68] However, their focus was mechanistic and not readily applied in contemporary clinical settings. Thus, although such approaches may become clinically feasible in the future, they were excluded from this mapping review. Twenty articles (representing 19 cohorts) meeting these criteria were identified, and key characteristics (ie, sample size, follow-up period, primary outcome, accuracy estimates, and base rates of recovery) are summarized in **Table 1**.[7–10,12,18,22,23,30,33,39,40,43,53,54,56,64,75,77,81]

2.2. Individual predictors

Predictor variables included in each cohort, whether they contributed statistically to the outcome of interest or not, are summarized in **Table 2**. These studies included predictors falling broadly into demographic, pain, general health, psychosocial, and occupational domains. The number and variety of predictors examined for LBP outcomes is substantial as is the lack of consistency across studies. We acknowledge that the inconsistency of predictors is likely due to researchers' goals for each analysis. **Table 2** also highlights areas that have been underrepresented as predictors, including comorbid conditions (2/20 articles) or health behaviors such as physical activity (7/20 articles). Another weakness of the current literature was that some relevant health behaviors were virtually unexplored (eg, alcohol use, drug use, and sleep disturbance) in the 20 articles included in this review.

2.3. Outcome measures

Outcomes examined in each study are summarized in **Table 3**. Most studies examined multiple outcome domains related to defining chronic LBP as an outcome. Functional disability was the most commonly reported outcome (9/20 articles), followed by work status or pain-related work absence (8/20 articles). Measures of pain presence (a dichotomous measure) or pain intensity (a continuous measure) were used as outcomes in 6/20 articles. Most studies defined and reported rates of recovery in terms of these pain outcomes.

2.4. Analytical approach

The review included 10 multivariate linear regression models for continuous outcomes. For categorical outcomes, there were 7 multivariate logistic regression models reported.

2.5. Prediction accuracy

Key study characteristics and factors that determined prediction accuracy for a given study (ie, variance accounted for, recovery base rate, recovery criterion, and classification summary) are summarized in **Table 1**. Only 1 of the linear regression models explained more than 50% variance in continuous outcomes. For the categorical outcomes, 5 of the 7 multivariate models reported classification accuracy higher than base rates. Base rates were calculated from the proportion of patients with acute or subacute back pain reporting they achieved recovery criterion at follow-up. The range for improvement of classification rates over base rate was 4% to 30%, with only one model reported improvement greater than 10% over the base rate of transition.

3. Current state of acute to chronic low back pain prediction

As expected, the mapping review identified considerable variety in individual measures used to predict the development of chronic LBP (**Table 2**). There are so many specific measures (or measurement tools) available for predictive modelling identified in the review that it is unlikely standardizing individual predictor variables will be feasible. However, the mapping review did identify opportunities for ensuring representation of each relevant predictor domain. This seems to be an important consideration for predictive frameworks to consider as many of the individual measures used across different studies for a given predictor domain are likely to be highly correlated (ie, different depressive symptom measures). Emphasizing consistency in predictor domain representation in predictive models may improve capabilities to compare model performance or pool data in future

Table 1

Study characteristics and accuracy of predicting low back pain outcomes.

Lead author	Year	PMID	Sample	Follow-up period	Primary outcome variable(s)	Variance accounted for	Recovery base rate	Recovery criteria	Odds ratios	Classification accuracy
Bousema	2007	17467902	124 subacute LBP patients	1 y	Change in physical activity/ fitness	—	30%	≥3 weeks without LBP	—	—
Burton	1995	7604349	120 acute LBP patients	1 y	RMDQ	69% (coping strategies, pain intensity, somatic perception, straight leg raise, and leg pain)	72%	RMDQ ≤2	—	82% (depression, coping strategy, pain radiating to leg, and straight leg raise test)
Burton	2004	14723859	120 acute LBP patients	4 yrs	RMDQ	—	—	RMDQ ≤2	—	—
Campbell	2013	23791041	488 acute LBP patients	5 yrs	Chronic pain grade (CPG)	—	—	CPG <2	Low social class (1.19) Baseline PI (1.09) Belief of high pain duration (1.06)	—
Cherkin	1996	9112715	219 acute LBP patients	1 y	Self-reported symptom satisfaction ("good" vs "poor")	—	71%	—	Depression (2.3) pain below knee (2.4)	—
Dionne	1997	9048688	569 LBP patients (training sample); 644 LBP patients (validation sample)	2 yrs	RMDQ	28% (depression, somatization, baseline RMDQ, and # pain days in past 6 mo)	84%	<50% of initial RMDQ	—	85% (depression and somatization)
Epping-Jordan	1998	9776000	78 acute LBP patients	1 y	Pain intensity (PI) Disability	32% (PI: baseline PI, demographics, baseline disability, and depression) 40% (disability: baseline disability, income, ethnicity, age, baseline PI, and depression)	—	—	—	—
Felicio	2017	28923172	135 women age 60+ with acute LBP	1 y	RMDQ Gait speed	11% (RMDQ: PI, age, BMI, education, and handgrip strength) 13% (gait speed: PI, age, BMI, education, and handgrip strength)	—	—	—	—
Gatchel	1995	8747248	421 acute LBP patients	1 y	Work status	—	87%	Return to work	—	91% (PI and disability, workers comp. status, gender, and MMPI scale 3)
Gheldof	2007	17314055	309 patients with 1–30 days of LBP in year before study, 253 w/>30 days of LBP in year before study	1 y	Days of LBP in previous year	—	—	<30 total days of LBP in year before follow-up	1 <LBP days <30 Baseline PI (1.19) Pain radiates to feet (2.92) Dynamic workload (0.63) Social support from coworkers (0.73) Fear of work-related activity (1.04) >30 LBP days Baseline pain intensity (1.18)	—

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Table 1 (*continued*)

Study characteristics and accuracy of predicting low back pain outcomes.

Lead author	Year	PMID	Sample	Follow-up period	Primary outcome variable(s)	Variance accounted for	Recovery base rate	Recovery criteria	Odds ratios	Classification accuracy
Grotle	2007	16677837	123 acute back pain patients	1 y	RMDQ	—	83%	RMDQ ≤4	High psychosocial risk (4.37) High emotional distress (3.30)	—
Haldorson	1998	9636972	260 subacute LBP patients on sick leave	1 y	Work status	—	77%	Return to work	—	71% (locus of control, lateral mobility, and work ability)
Henschke	2008	18614473	973 acute LBP patients	1 y	Pain intensity Disability Work status	—	57% 75% 94%	≥1 month pain-free, without disability, and returned to work	—	—
Klenerman	1995	7747233	196 acute LBP patients	1 y	Combined pain and disability	32% (demographic, medical history, and fear-avoidance variables)	93%	Patient report of intermittent or no pain	—	88% (demographic, medical history, and fear-avoidance variables)
Koleck	2006	16291293	99 acute LBP patients	1 y	Functional nonadjustment Emotional nonadjustment	43% (functional nonadjustment: sex, history of LBP, and inactivity) 23% (emotional nonadjustment: Trait depression)	67%	Self-report of symptom resolution	—	—
Law	2013	23179745	241 acute/subacute LBP patients	1 y	Work status Sick leave duration	— —	71% 46%	≥4-week work in last year <30-day sick leave in last year	Baseline PI (0.82) OMPQ (0.98) OMPQ (1.03) Fear avoidance (1.02)	50%, 82% (work status: OMPQ cutoffs of 105 and 130) 76%, 34% (Sick leave duration: OMPQ cutoffs of 105 and 30)
Machado	2016	27503263	999 acute LBP patients	1 y	Pain intensity Work interference	—	72% 88%	≤3-month duration <12-month duration	Manual task-related factors (4.0–13.0) Moderate/vigorous physical activity (4.0) Fatigue (2.0)	—
Schiottz-Christensen	1999	10439974	503 acute LBP patients	1 y	Quality of outcome (poor, fair, or good) based on Px questionnaire	—	82% "Fair" 52% "Good"	Patient perception of LBP resolution, return to work, and function	Previous sick leave due to LBP (2.30) Disabled by LBP (2.40) Physician assessment of susceptibility to chronic LBP (3.70–10.40)	—
Sieben	2005	16099095	222 acute LBP patients	1 y	Graded chronic pain scale (GCPS)	26% (demographics, history of LBP, and baseline PI)	—	GCPS >2	# Previous episodes (2.17) Baseline PI (1.02)	—
Truchon	2012	21796374	535 injured workers (subacute LBP)	1 y	Work absence	12% (work-related fear avoidance, return to work expectation, income, education, irregular work schedule, and work concerns)	62%	Work absence ≤182 days	—	73% (fear avoidance, return to work expectation, income, education, and work schedule/concerns)

LBP, low back pain; OMPQ, Orebro Musculoskeletal Pain Questionnaire; RMDQ, Roland-Morris Disability Questionnaire.

Table 2

Predictors of chronic low back pain examined in longitudinal studies of at least 12-month duration.

Predictors	Bousema 2007	Burton, 1995/ 2004	Campbell, 2013	Cherkin, 1996	Dionne, 1997	Epping-Jordan, 1998	Felicio, 2017	Gatchel, 1995	Gheldof, 2007	Grotle, 2007	Haldorson, 1998	Henschke, 2008	Klenerman, 1995	Koleck, 2006	Law, 2013	Machado, 2016	Schiottz-Christensen, 1999	Sieben, 2005	Truchon, 2012
Demographic																			
Age	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	
Sex	X	X	X	X	X			X	X	X	X	X	X	X	X		X	X	
Race/ethnicity				X	X	X		X				X							
Education			X	X	X	X	X	X	X	X	X	X						X	X
Income/class			X		X	X					X	X		X					X
Marital status				X	X	X		X			X		X	X			X		X
Children					X						X			X					X
Household size					X														
Living arrangement					X						X								
Pain																			
Intensity	X	X	X		X	X	X	X	X			X	X	X	X			X	X
Duration		X	X	X	X			X		X	X	X	X				X	X	
Disability	X	X	X	X	X	X		X		X	X	X	X		X				X
Onset (sudden/ gradual)										X		X					X	X	
Radiating		X	X	X	X	X			X	X		X					X	X	X
Previous pain episodes		X		X	X				X	X		X	X	X			X	X	
Chronic pain grade				X	X														
Function (eg, leg raises)		X					X			X	X	X	X				X		
Neurological signs						X				X			X				X		
Pain medication										X		X							
Related to injury or work					X							X					X		
Other characteristics		X		X	X	X					X	X	X		X		X	X	X
Health																			
Sleep medication/ sleep quality										X									X
Smoking				X	X				X	X	X	X	X						
Alcohol					X											X			
General health perception				X	X				X		X	X							
Comorbid diseases					X					X									
BMI/obesity status					X		X		X				X	X			X		
Activity	X								X		X	X		X		X		X	
Psychosocial																			
Coping strategies		X	X									X	X	X				X	X
Perceived Control/ LOC		X			X						X			X					
Expectation for chronicity			X		X							X					X		
TSK	X		X						X									X	

(*continued on next page*)

Table 2 (*continued*)

Predictors of chronic low back pain examined in longitudinal studies of at least 12-month duration.

Predictors	Bousema 2007	Burton, 1995/ 2004	Campbell, 2013	Cherkin, 1996	Dionne, 1997	Epping-Jordan, 1998	Felicio, 2017	Gatchel, 1995	Gheldof, 2007	Grotle, 2007	Haldorson, 1998	Henschke, 2008	Klenerman, 1995	Koleck, 2006	Law, 2013	Machado, 2016	Schiottz-Christensen, 1999	Sieben, 2005	Truchon, 2012
FABQ		X							X	X					X				X
Somatization or somatic awareness		X			X								X						
Catastrophizing	X				X														X
MPQ		X																	
PSEQ			X																
DRAM		X																	
IPQ-R			X																
ALBPSQ/OMPQ										X					X				
Stressful life events					X								X						
Social support											X			X					
Quality of life														X					
Anxiety			X								X	X		X					X
Depression	X	X	X	X	X	X						X	X	X				X	X
Negative affect									X	X								X	
Psychological diagnosis					X			X											
Personality								X			X								
Other				X					X	X		X				X	X		
Occupational																			
Status	X		X	X	X					X		X	X				X	X	
Satisfaction				X					X	X				X				X	X
Absence due to LBP																	X	X	X
Type of work					X														
Shift work/irregular schedule									X										X
Years at job					X						X								
Physical demands				X	X				X		X					X			X
Psychological demands									X										X
Work load/travel time											X								
Other work-related factors																			X
Workers' compensation or personal injury case				X	X							X							
Housekeeping responsibilities					X														

ALBPSQ, Acute Low Back Pain Screening Questionnaire; DRAM, Distress and Risk Management Method; FABQ, Fear-Avoidance Beliefs Questionnaire; IPQ-R, Illness Perception Questionnaire-Revised; LBP, low back pain; LOC, locus of control; MPQ, McGill Pain Questionnaire; OMPQ, Orebro musculoskeletal pain questionnaire; PSEQ, Pain Self-Efficacy Questionnaire; TSK, Tampa Scale for Kinesiophobia.

Table 3

Low back pain outcomes examined in longitudinal studies of at least 12-month duration.

Outcomes	Bousema, 2007	Burton, 1995/2004	Campbell, 2013	Cherkin, 1996	Dionne, 1997	Epping-Jordan, 1998	Felicio, 2017	Gatchel, 1995	Gheldof, 2007	Grotle, 2007	Haldorson, 1998	Henschke, 2008	Klenerman, 1995	Koleck, 2006	Law, 2013	Machado, 2016	Schiottz-Christensen, 1999	Sieben, 2005	Truchon, 2012
Functional disability		X/X			X	X	X			X		X	X	X			X		
Pain presence/ intensity		X/X				X				X		X	X			X			
Work status								X			X	X			X		X		
Work absence										X				X	X		X		X
Chronic pain grade			X															X	
Psych. distress, anxiety, and depression						X								X					
Activity/fitness	X																		
Care seeking		X/X												X					
Gait speed							X												
Days with LBP									X										
Subjective improvement																	X		
Symptom satisfaction				X															
General health perception														X					
Work interference																X			

LBP, low back pain.

analyses. All predictive models included in the mapping review incorporated baseline predictive measures. There may be justification for including select time-varying elements as models that incorporate both static (eg, age, sex, and socioeconomic status) and selected time-varying elements (eg, changes in pain, disability, or psychological distress.[6,32]) may improve prediction accuracy.

The studies included in the mapping review used a wide variety of outcome measures. This does not necessarily indicate a problematic lack of standardization between studies because choice of outcome measures depends on specific research goals. A study focused on the impact of back pain on inability to work should include return to work as the primary outcome measure. However, such a focus prevents progress in identifying predictive factors that generalize to other outcomes relevant to the development of chronic LBP. For example, a model designed specifically for accurate prediction of pain intensity may not be well suited for predicting disability or patient satisfaction.[48] Instead of having a given predictive approach linked to one outcome, there is an opportunity to test a standardized predictive framework across multiple outcome measures that are representative of chronic LBP. Testing the same predictive model for accuracy across multiple outcomes will avoid over specification of predictive approaches (ie, needing separate predictive models for each outcome of interest), and in the process of being simpler to implement, a single predictive framework may have a broader impact for informing clinical decision making.

Given that most of the approaches included in the mapping review incorporated linear or logistic regression, there is an opportunity to explore if novel analytical approaches have the potential to improve prediction accuracy. In particular, novel approaches that leverage machine learning and artificial intelligence methods that identify patterns in care and account for the emergent and dynamic nature of chronic LBP pain development may improve identification of those at risk. Finally, and perhaps the most obvious indicator that new predictive approaches need to be considered, during the 21-year period covered by this mapping review, there was no trend of improved predictive accuracy.

4. Proposed framework for improving prediction of transition from acute to chronic low back pain

The proposed framework for improving prediction of acute to chronic LBP is described in **Figure 1** and presented in more detail in the subsequent sections.

4.1. Standard predictor domains

Previous predictive studies in LBP have considerable variability in demographic, pain, health, psychosocial, and occupational domains. One problem with the use of this many domains is that any one particular study very rarely had representation from each predictor domain. In response, we are including standardized predictor domains in the proposed framework. Standardized predictor domains will allow for better direct comparison of predictive accuracy and also allow for models to be tested for accuracy across multiple outcomes representative of development of chronic LBP.

Although domain standardization is emphasized in this framework, the specific measures used remain an important issue to consider. One important issue is to ensure including measures representing both modifiable and are considered direct treatment targets (eg, baseline pain intensity), as well as nonmodifiable factors for whom treatments can be tailored (eg, age, since care approaches may differ for younger vs older patients). A robust predictive framework will include a mix of modifiable and nonmodifiable factors with the goal of maximizing potential of predictive accuracy for chronic LBP development. Another important consideration is that the specific measures must be pragmatic for capture using electronic health record, and not greatly increase patient or provider burden. Therefore, to improve likelihood for successful implementation, it is recommended that a minimum set of variables be used to represent each domain.

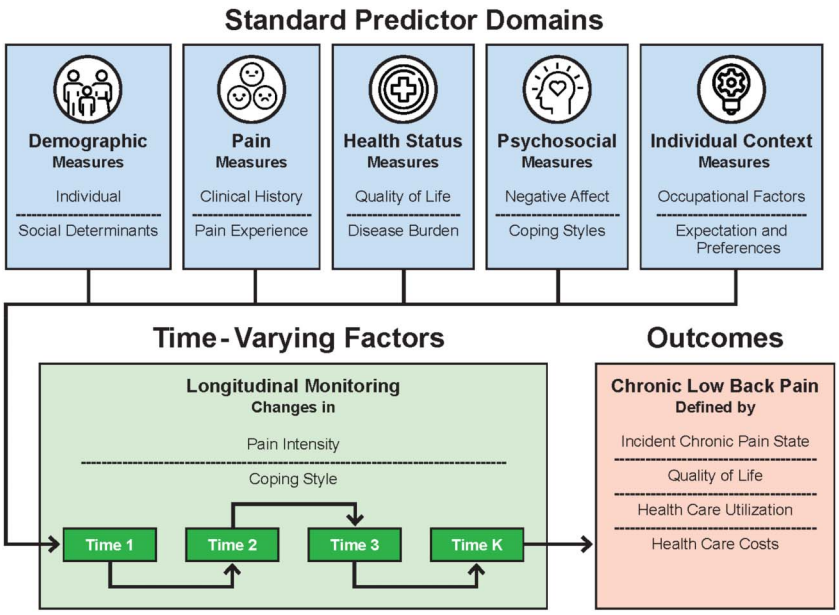

Figure 1. Predictive framework for predicting transition from acute to chronic low back pain.

4.2. Minimum variable set for each predictor domain

Representing the *demographic domain* are variables capturing individual characteristics and social determinants of health. Individual characteristics in the demographic domain are commonly captured in studies predicting MSK outcomes often including age, sex, gender, race, and ethnicity. However, social determinants of health are not often included, and emerging evidence suggests that valuable insights can be gained from this predictor. For example, having Medicaid coverage was an independent predictor of poorer LBP outcomes in a cohort study when compared with a validated LBP screening tool,[50] whereas lower education and income levels decreased the positive effects of psychologically informed stratified care in a randomized trial.[5]

Recommended specific measures for the *pain domain* are variables representing clinical history (eg, duration of symptoms and history of previous conditions) and the pain experience (eg, anatomical location, pain severity, and pain impact). The pain domain has been frequently included in previous studies, often as measures of pain intensity or duration. However, to improve predictive accuracy, it may be necessary to have broader representation of this domain. For example, a recent study has indicated that multiple sites of pain can be predictive of poorer LBP outcomes.[74] Adequate representation of the pain domain beyond intensity and duration is necessary to allow for clear determination of which characteristics of the pain experience have strong and consistent temporal associations with the development of chronic LBP.

The *health status domain* is not commonly represented in longitudinal studies predicting MSK pain outcomes. Therefore, it is important to adequately represent this domain in future predictive studies. Recommended specific measures for representing this domain are variables for health-related quality of life (eg, functional status and mental health) and disease burden (eg, comorbidity) measures. Quality of life measures are well established in the study of LBP; however, comorbidity measures have not been commonly used. Comorbidity represents an emerging area of interest for the prediction of chronic LBP. Measuring comorbidity number is the current standard, as demonstrated in a recent cohort analysis indicating lower comorbidity was protective of having persistent pain 12 months after seeking physical therapy care for a variety of musculoskeletal pain conditions, including LBP.[6] Approaches that systematically consider comorbidity in addition to number will allow for broader consideration of disease impact and may lead to better accuracy for prediction of LBP outcomes.

The *psychosocial domain* has been highly studied in prediction of LBP outcomes. This domain includes the cognitive, affective, and behavioral aspects, and collectively, the psychosocial domain has been used to determine the overall level of distress associated with LBP. Many different individual psychosocial measures have been studied, and they can be broadly categorized into negative affect (eg, depressive symptoms and anxiety) and coping styles (eg, fear avoidance, pain catastrophizing, and self-efficacy). Psychosocial measures consistently predict LBP outcomes in cohort studies.[6,26,32] However, head to head comparisons of commonly used screening tools indicate statistical similarity, making recommendation of a specific measurement approach difficult because there is no superior single measure.[3,48,49] Instead, it seems important to ensure the measures used capture negative mood and coping styles, and both negative (eg, fear avoidance and catastrophizing) and positive (eg, self-efficacy and acceptance) coping are measured to represent this domain.[58]

The final domain to consider in this predictive framework is the *individual context domain*. As per the mapping review, specific measures recommended for this domain have included occupational factors (eg, job satisfaction and perceived work stress). By contrast, for nonoccupational cohorts, this domain has not been well represented. Therefore, it will be necessary to represent this domain with specific measures that capture the perceptions of receiving care, including patient expectations and treatment preferences. For example, a validated prediction tool for the development of chronic LBP included one item on the expectation of having persistent pain in its final 5-item version.[79] Beyond that example, the individual context domain has been largely unexplored in the transition from acute to chronic LBP prediction studies. Including this a standardized domain in future studies could be an important way to improve prediction accuracy.[55]

4.3. Time-varying factors

Traditionally, prediction of LBP outcomes has included static, baseline determinants of risk. The primary limitation with this approach is that it does not account for any time-varying factors of the care episode that may indicate change in the initial risk status.[21,42] Static risk determination may be an acceptable strategy for certain nonmodifiable factors; however, it inherently limits the impact modifiable, time-varying factors have on outcome prediction. Without accounting for such changes in modifiable factors, predictive models cannot distinguish between an outcome driven by an overall poor prognosis vs an initial poor treatment response. Models that account for this distinction by including static and time-varying factors are important for advancing LBP outcome prediction.

Recent evidence from LBP studies have demonstrated that predictive approaches allowing for early changes that occur when receiving health care can improve predictive accuracy for treatment outcomes.[4,32,83] This process has been described as "treatment monitoring," and in LBP, it often accounts for changes in the psychosocial domain to improve on baseline risk determination.[4,32,83] However, since not all studies will involve care seeking cohorts or monitoring could continue following the end of formal treatment, the term "longitudinal monitoring" will be used in this framework to describe the capture of time-varying factors. Psychosocial measures are the most obvious choice for longitudinal monitoring, given the current state of the literature. There are likely other time-varying measures that can be used for longitudinal monitoring; however, these have not been clearly identified as this line of research is still emerging. Accounting for longitudinal monitoring in predictive models does increase the burden of data collection, as capturing multiple, patient-level time points are required. However, collection of these factors need not be comprehensive, should be driven by empirical evidence, and may be amenable to use of mobile applications or wearable technology.[16] For instance, several treatment mediators[57,66,67] for LBP outcomes have already been identified, and many of these are from the psychosocial (eg, fear avoidance and self-efficacy) or pain (eg, pain intensity) domains. Therefore, only these variables would be included in predictive models until other time-varying factors are confirmed through external validation studies.

4.4. Outcomes

There are multiple definitions of chronic pain in the literature, yet no one definition is widely enough accepted to be considered as a standard.[80] Recent *International Classification of Disease*

recommendations provide diagnostic codes from chronic pain as a primary condition[70] and also codes for secondary conditions such as musculoskeletal[71] or postoperative pain.[76] These diagnostic codes will be very helpful in identifying those that already have chronic pain, but these codes do not directly address which outcome measures should be used for predicting acute to chronic LBP transitions. The lack of standard definitions for what constitutes chronic LBP means there is a need for different perspectives on which specific measures should be used to define chronic LBP. At a minimum, the patient, provider, and payer perspectives should be considered because there is an expectation that the most robust definitions of chronic LBP will be a convergence of these perspectives. This means that prediction models will need to be flexible to allow for the prediction of different definitions of chronic LBP and not any one measure alone.[59] This creates the need for the accuracy of a given predictive model to be simultaneously tested across multiple outcome measures, a different approach than was identified in the mapping review (ie, most studies had single primary outcome). Outcomes that can be used to accommodate multiple definitions of chronic LBP are a priority in this predictive framework and include (1) incident chronic pain state, (2) quality of life, (3) health care utilization, and (4) health care costs. The capture of these outcomes, while not exhaustive, would provide enough information to meet multiple definitions of chronic LBP and thereby providing better support to subsequent clinical, policy, and public health actions.

5. Implementation of predictive framework for predicting low back pain outcomes

5.1. Application example

The National Institutes of Health (United States) Pain Consortium convened a Research Task Force for chronic LBP in 2009 to 2010. The charge of the Research Task Force was to review definitions, diagnostic criteria, and outcome measures for clinical research, develop a draft set of standards for research on chronic LBP, and engage the research community and government agencies in developing research standards. The Research Task Force disseminated their recommendations, which included a minimal data to support research standards.[17] This minimal data set can be used as an application example for this predictive framework, while fully acknowledging there is a much larger pool of potential measures available. Following the Research Task Force, recommendations has the advantages of including measures already vetted and endorsed by an expert, multidisciplinary panel, and emphasizing a pragmatic approach by including a standard data set that may make this framework easier to implement in real-world settings.

The Research Task Force minimal data set includes 40 items; many derived from previously validated questionnaires like the Start Back Screening Tool and Patient Reported Outcome Measurement Information System domains.[17] The minimal data set was designed to be broad enough to capture domains applicable to stakeholder groups including patients, providers, and policy makers. In **Table 4**, we have listed each of the Research Task Force's items and indicated how they could be represented as predictor or outcome domains in this predictive framework. There is coverage of these domains by minimal data set items, consistent with the Research Task Force's charge. Therefore, practitioners or researchers looking to adopt this predictive framework could use the Research Task Force's minimal data set as a starting point for implementation in their setting.

There are, of course, caveats to consider when using the Research Task Force's minimal data set within this predictive framework. First, there are some measures considered as both predictors and outcomes in **Table 4**. This may be entirely appropriate given the research question (eg, knowing the present pain state to predict a future pain state); however, care must be taken when interpreting models that include the same measures as both predictors (ie, independent variables) and outcomes (ie, dependent variables). One potential way to address this issue is to compare prediction characteristics of models with and without the baseline dependent variable included to inform the impact on prediction accuracy. Second, **Table 4** shows there are certain domains that may be better represented with additional measures beyond the Research Task Force's recommendations. Although several items in the minimal data set could be used as time-varying factors, it may be better to have full-length questionnaires representing this domain as they are more sensitive to change (eg, instead of using one item from the Pain Catastrophizing Scale would use the entire questionnaire for longitudinal monitoring). This line of research (ie, time-varying factors and associated psychometric properties) is still emerging, and we have cite several examples for those interested in more details.[4,32,83] The context domain was only represented by 3 items (**Table 4**), and these items were specific to those with LBP that was work-related or having legal involvement. These are important factors to capture, but researchers interested in other contextual issues (eg, treatment expectations and health care system characteristics) would need to include additional measures. Collectively, these caveats provide examples of how the Research Task Force's recommendations can be adapted to better address specific research questions while applying the proposed predictive framework.

5.2. Analytical considerations

There is growing interest in the use of machine learning methods to improve the health of patients by identifying latent patterns in data that can aid in prediction.[25] Machine learning is a subset of artificial intelligence that aims to train computers (ie, machines) to improve the performance of tasks such as prediction through supervised, semisupervised, and unsupervised approaches. Machine learning–based approaches can address some of the limitations of traditional regression approaches, including nonlinearities, heterogeneity of effects (ie, interactions), and numerous, complex predictor variables.[36] They can also be used to address missing data, which are common in studies conducted using administrative and health record data. To be sure, data are only collected when patients interact with health systems, and previous work has shown that this interaction can impact inference[72] and risk prediction.[82] Machine learning–based imputation methods, such as multilayer perceptron, k-nearest neighbor, and self-organization maps have been shown to outperform traditional statistical approaches for risk prediction.[47,82] However, these approaches are not commonly used in LBP research to address missing data. Common machine learning methods used in pain research include classification for clinical diagnosis, structure detection to identify clusters of patients, and knowledge discovery to discover patterns in clinical data. Specifically, it has been proposed that areas where machine learning–based approaches may impact pain research the most include phenotyping and classifying pain,[11,63] predicting outcomes of interventions to address pain,[84] and differentiating pain from other physiological signals.[46]

Table 4

Application of predictive framework with the National Institutes of Health chronic low back pain research task force recommendations for a minimal data set.

NIH LBP task force	Predictor domains					Outcome domains			
Minimal data set item	Demographic	Pain	Health status	Psychosocial	Context	Pain states	Quality of life	Care utilization	Care costs
1. How long has low back pain been an ongoing problem for you?		X				X			
2. How often has low back pain been an ongoing problem for you over the past 6 months?		X				X			
3. In the past 7 days, how would you rate your low back pain on average?		X				X			
4. Has back pain spread down your leg(s) during the past 2 weeks		X							
5. During the past 4 weeks, how much have you been bothered by…			X						
6. Have you ever had a low back operation?		X						X	X
7. If yes, when was your last back operation?		X						X	X
8. Did any of your back operations involve a spinal fusion? (also called an arthrodesis)		X						X	X
9. In the past 7 days, how much did pain interfere with your day-to-day activities?			X				X		
10. In the past 7 days, how much did pain interfere with work around the home?			X				X		
11. In the past 7 days, how much did pain interfere with your ability to participate in social activities?			X				X		
12. In the past 7 days, how much did pain interfere with your household chores?			X				X		
13. Have you used any of the following treatments for your back pain? (Check all that apply)		X						X	X
14. I have been off work or unemployed for 1 month or more due to low back pain.					X				
15. I receive or have applied for disability or workers' compensation benefits because I am unable to work due to low back pain.					X				
16. Are you able to do chores such as vacuuming or yard work?			X						
17. Are you able to go up and down stairs at a normal pace?			X						
18. Are you able to go for a walk of at least 15 minutes?			X						
19. Are you able to run errands and shop?			X						
20. In the past 7 days, I felt worthless				X					
21. In the past 7 days, I felt helpless				X					
22. In the past 7 days, I felt depressed				X					
23. In the past 7 days, I felt hopeless				X					
24. In the past 7 days, my sleep quality was				X					
25. In the past 7 days, my sleep was refreshing				X					
26. In the past 7 days, I had a problem with my sleep				X					
27. In the past 7 days, I had difficulty falling asleep				X					
28. In the past 7 days, it's not really safe for a person with my back problem to be physically active				X					
29. I feel that my back pain is terrible and it's never going to get any better				X					
30. Are you involved in a lawsuit or legal claim related to your back problem?					X				
31. Have you drunk or used drugs more than you meant to?	X								
32. Have you felt you wanted or needed to cut down on your drinking or drug use?	X								
33. Age:	X								
34. Gender:	X								
35. Ethnicity	X								
36. Race:	X								
37. Employment status	X								
38. Education level	X								
39. How would you describe your cigarette smoking?	X								
40. Height and weight	X								

LBP, low back pain.

Although there is a need to consider machine learning approaches in future predictive modeling, there is also the need to ensure they are adequately tested against traditional approaches. For example, in risk prediction models for mortality for patients receiving hemodialysis, there was no advantage of more complex approaches (eg, machine learning) when a range of statistical approaches were considered.[37] In a systematic review of clinical prediction models across a variety of practice areas and including studies with a wide range of sample sizes, machine learning (ie, classification trees, random forests, artificial neural networks, and support vector machines) was compared with logistic regression.[14] For the 71 studies included in this review, there was no evidence of better prediction performance for the machine learning approaches. Therefore, while consideration of advance analytical approaches is necessary to determine whether their use results in better predictive accuracy than identified in our mapping review, it cannot be assumed that machine learning approaches will always outperform traditional approaches for improved accuracy.

Another important aspect of prediction models for chronic LBP outcomes—whether derived through traditional or novel analytical approaches—is the need for validation across multiple health systems. Models developed in a single health system may not have the same prediction characteristics as models that are validated across multiple health systems. This is of particular importance because there is increasing interest and need to leverage real-world data for predicting LBP outcomes, yet most approaches are developed and validated in a single health system using a cohort approach. This can be problematic for generalization of predictive models because previous research in other clinical areas has shown that patients recruited through cohort studies and clinical trials are not necessarily representative of real-world patients.[52] As the volume and velocity of real-world data increases, great care must be taken to validate results generated from a single health system to determine how useful that predictive framework will be in other health systems. Available data resources in the United States that might be helpful for establishing the generalizability of findings within specific health systems include the American Physical Therapy Association's Outcomes Registry, commercial payer databases (eg, Optum Labs, MarketScan), and publicly available population-based data sets (eg, Medical Expenditures Panel Survey, and National Health and Nutrition Examination Survey). For example, retrospective cohort data from commercially insured US adults have been used to identify how early exposure to nonpharmacological providers limits short- and long-term opioid use for those with LBP[51] and establishing the risk of serious infection among users of biologics for psoriasis and psoriatic arthritis.[62]

6. How this predictive framework will advance research and practice

This review presented a framework that could be used in future studies to improve predictive modeling approaches for studying the transition from acute to chronic LBP pain. The predictive approach proposed in **Figure 1** promotes standardization of predictor domains and multiple outcome measures that represent chronic LBP. This framework provides the opportunity to develop and test models in a structured manner to determine whether improvements in predictive accuracy occur. The framework was developed to be used as a companion to recommendations for improving methodological reporting of predictive studies, for example, the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) statement.[15] Awareness of the TRIPOD statement will ensure those studying the transition from acute to chronic LBP report the essential methodological elements of predictive studies, which are often missing when the models are published.[44] The emphasis on standardizing predictive domains provides flexibility for this framework to be adapted for widespread testing in the electronic health record. This predictive framework provides directions for approaches that can be adopted and integrated into the electronic health record, so that it evolves past being an administrative platform to a critical component of learning health systems. Widespread testing will result in validation and refinement to prediction models that improve accuracy and the development of clinical decision aids that could be used to support treatments that better limit the transition from acute to chronic LBP.

Improving the prediction accuracy of the transition to chronic LBP is strongly aligned with recent clinical practice guidelines[19,73] and the Federal Pain Research Strategy (United States).[31] Refined prediction can enhance value of care by identifying individuals appropriate for condensed care episodes or alternative delivery options that are less resource intensive (eg, telehealth options) based on their risk of developing chronic LBP. For instance, patients in a care pathway designed to accommodate a low risk to transition to chronic LBP may be appropriate for exposure to a variety of nonpharmacological treatments. This low-risk pathway would also have strict criteria for escalation to care options that have higher risk and no guarantee of additional benefit (eg, injections, opioids, or surgery) because the overall prognosis is generally favorable. By contrast, patients in a high risk to transition to chronic LBP pathway would be more closely monitored with pain and quality of life measures, so that timely and appropriate systematic decisions could be made for care escalation.

Early and accurate prediction of the development of chronic LBP will allow for efficient distribution of health care resources at the initial point of care. For LBP, this initial point of care is extremely important because it can have dramatic effects on downstream pain-related outcomes, health care utilization, and costs.[28,29] In this manner, the updated predictive framework would facilitate delivering value by aligning effective care with utilization and cost resources, consistent with the Institute for Healthcare Improvement Triple Aim Initiative.[59] More efficient resource allocation can only be accomplished by more accurate identification of individuals that are going to subsequently resolve their acute pain condition vs those that are going to progress into a chronic condition.

Existing predictive approaches for chronic LBP outcomes did not incorporate time-varying, modifiable factors to refine outcome prediction. The proposed predictive framework adds time-varying factors through longitudinal monitoring, consistent with the literature citing the importance of treatment mediators[57,66,67] and the type of monitoring that has already been previously described for LBP.[4,32,83] This addition is burdensome, and in that it adds another data collection point beyond baseline, but it is a necessary step to prepare for moving toward dynamic modeling of LBP pain outcomes. There is already evidence supporting dynamic models to predict outcome of other chronic nervous system diseases, including incident Alzheimer's and Huntington's Disease.[60,61] Implementation of this predictive framework will enable development of similar approaches to predict incident chronic LBP. Dynamic predictive models allow for learning health systems in which multiple time points can be used to more accurately determine risk status, with care options adjusted in real time. For example, a short-term decrease in pain after exercise therapy that is indicative of long-term recovery from back pain may result in a real-time decision to delay spine surgery or avoid use of prescription opioids.

Finally, improved accuracy in outcome prediction could reduce uncertainty surrounding optimal LBP management strategies. This uncertainty is driven by multiple pharmacological and

nonpharmacological treatment options that have very similar treatment effects.[13,78] This lack of treatment superiority for any given treatment option clouds clinical decision-making. It is likely that this lack of definitive treatment superiority contributes to the unwarranted variability in health care delivery observed for LBP. A validated prediction framework could ultimately reduce this uncertainty (and the associated care variability) moot by providing accurate long-term estimation of developing a chronic pain state. Interestingly, empirically based approaches for predicting outcomes have been used in other areas of medicine, including watchful waiting in prostate cancer[20] or shared decision-making for left ventricular assist device in heart failure.[1,69] For LBP, there is potential for predictive models with increased accuracy to advance care decision-making in similar ways, either by routine monitoring of patients to assure an initial prognosis remains favorable or by using the likelihood of chronic LBP development to inform the length and intensity of a care plan. Importantly, we present a framework for enhanced prediction, but this framework is not intended to result in the development of static models. As additional potential predictors are identified, particularly those amenable to large scale application in real-world settings (eg, neuroimaging of brain structure or function becomes more common), we expect predictive models to continue to grow and evolve, as they work to meet a goal of optimized predictive accuracy.

7. Conclusion

Predictive approaches for the transition from acute to chronic LBP pain need to improve to meet practice and research priorities from clinical guidelines[19,73] and the Federal Pain Research Strategy (United States).[31] This review presented a predictive framework that improves upon previous approaches by standardizing predictor domains and encouraging use of multiple outcome measures to represent chronic LBP. There is potential that this predictive framework could lead to improvements in predictive accuracy that has not occurred naturally over time. However, empirical testing of this framework is necessary to determine whether it actually improves predictive accuracy, and whether advanced analytical approaches outperform traditional statistical approaches.

Disclosures

The authors have no conflicts of interest to declare.

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