

Prognostic value of quantitative sensory testing in low back pain: a systematic review of the literature

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Abstract: Quantitative sensory testing (QST) measures have recently been shown to predict outcomes in various musculoskeletal and pain conditions. The aim of this systematic review was to summarize the emerging body of evidence investigating the prognostic value of QST measures in people with low back pain (LBP). The protocol for this review was prospectively registered on the International Prospective Register of Systematic Reviews. An electronic search of six databases was conducted from inception to October 2015. Experts in the field were contacted to retrieve additional unpublished data. Studies were included if they were prospective longitudinal in design, assessed at least one QST measure in people with LBP, assessed LBP status at follow-up, and reported the association of QST data with LBP status at follow-up. Statistical pooling of results was not possible due to heterogeneity between studies. Of 6,408 references screened after duplicates removed, three studies were finally included. None of them reported a significant association between the QST measures assessed and the LBP outcome. Three areas at high risk of bias were identified which potentially compromise the validity of these results. Due to the paucity of available studies and the methodological shortcomings identified, it remains unknown whether QST measures are predictive of outcome in LBP.

Keywords: prognosis, quantitative sensory testing, low back pain, cohort studies, pain, sensory testing

Introduction

The course of low back pain (LBP) is typically characterized by symptoms subsiding quickly within the first 4–6 weeks, but for some people there is little improvement thereafter.¹ It has been estimated that up to 65% of people presenting to primary care for treatment of an episode of LBP still experience pain after 1 year.² Persistent LBP has been identified as the world's leading cause of disability³ and remains a challenge in clinical management.⁴ Determining which factors predict outcomes in LBP would allow the identification of people at high risk of poor outcomes for whom early, targeted interventions could be beneficial. Several studies have evaluated the contribution of clinical, demographic, and psychosocial factors on functional recovery after LBP,^{5–8} but previous attempts to synthesize this body of research have led to inconsistent conclusions about which set of factors are useful for prognosis of LBP.⁹ Reasons for this uncertainty may include methodological limitations of the study design.¹⁰ However, another reason might be that we lack knowledge about potential factors that can provide useful prognostic information for LBP.

The prognostic value of quantitative sensory testing (QST) measures has more recently been investigated in musculoskeletal pain conditions. For example, cold and

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mechanical pain hypersensitivity (pressure pain) have been shown to predict those at risk of poor outcome in both whip-lash injury^{11–13} and lateral epicondylalgia.¹⁴ Evidence from cross-sectional studies has shown that specific QST measures can discriminate between people with chronic LBP and healthy controls.^{15–18} Further, we know that some abnormal QST findings can be detected soon after the onset of LBP.¹⁹ However, to date, there has been no review of the literature investigating the prognostic value of QST measures in LBP.

The aim of this systematic review is to identify, evaluate, and summarize the emerging body of literature investigating the prognostic ability of QST responses in LBP.

Methods

Procedure

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement guidelines.²⁰ The protocol for this systematic review was prospectively registered on International Prospective Register of Systematic Reviews 2015 (registration number: CRD42015027228). Electronic searches for articles were conducted using the following databases from inception to October 2015: Ovid Medline, Ovid EMBASE, Ovid PsycINFO, Ovid Mantis, and Scopus. The PubMed database was also searched from January 2015 to October 2015 to retrieve recent literature not yet indexed in other databases. A comprehensive search strategy was designed with the assistance of an experienced research librarian and adjusted to account for differences in indexing across databases (Ovid Medline search is presented in Table S1). The search encompassed terms for the three domains of interest: LBP, QST, and prognosis. Terms for each domain were combined using the “AND” operator. The updated search strategy of the Cochrane Back Review Group 2013²¹ was used to identify back pain terms, while relevant terms for prognosis were based on those suggested by Altman¹⁰ and Hayden.²² Reference lists of the included studies were screened to track other relevant literature. In addition, 21 experts in the field were contacted to identify any studies we had missed or to retrieve additional results from unpublished data. Non-English language studies, where a translation could be made available, were included.

Study selection

We included prospective longitudinal studies based on the following criteria: adults at least 18 years or older with acute (<6 weeks), subacute (6–12 weeks), or chronic (>12 weeks) nonspecific LBP with or without leg pain;²³ participants had been assessed by at least one QST measure; LBP status

at follow-up was reported; the association between QST responses at baseline and LBP outcomes at follow-up was reported; and the follow-up duration was a minimum of 1 week. No restrictions were placed on the setting or recruitment source of participants. We excluded LBP due to serious pathology (eg, fracture, neoplasm, and infection) or a specific condition (eg, rheumatoid arthritis, failed back surgery syndrome, pregnancy, postpartum back pain, and chronic widespread pain such as in fibromyalgia, irritable bowel syndrome) or after back surgery. Studies that investigated LBP together with other musculoskeletal pain disorders (eg, neck pain and thoracic pain) were also included if at least >75% of the sample had LBP, or if data for LBP could be extracted separately.

The prognostic factors of interest were QST responses. The term QST was broadly used in this review to include psychophysical as well as specific electrophysiological tests. Psychophysical tests included “static” measures (eg, threshold determination to noxious and non-noxious stimuli and pain magnitude rating to suprathreshold stimuli) as well as “dynamic” measures (eg, temporal summation, conditioned pain modulation [CPM], and offset analgesia).²⁴ Specific electrophysiological tests included assessment of nociceptive reflexes (eg, nociceptive withdrawal reflex).

The outcomes of interest were measures of LBP status at follow-up, including pain intensity, functional status or disability, work status, health-related quality of life, and global perceived effect/recovery.

Study inclusion

After removal of duplicate papers, studies that met the inclusion criteria were independently screened by two reviewers based on the title and then abstract. Finally, full-text articles were assessed for inclusion independently by two reviewers using a piloted standardized eligibility sheet, and any disagreements were resolved by discussion and consensus, and with the assistance of a third reviewer at all stages of screening. Reference lists of the included papers were screened to locate other relevant articles. Further, 21 experts in the field were contacted by email to retrieve any additional published or unpublished data.

Risk of bias assessment

The risk of bias was assessed independently by two reviewers using the Quality in Prognostic Studies tool developed by Hayden et al²⁵ which was adapted for the needs of this systematic review, and incorporated additional criteria for assessment of bias in prognostic studies from other

sources.^{10,26,27} Each of the six domains comprised multiple items that were individually scored as “yes”, “no”, “unclear”, or “not applicable” and comments to support judgment were provided. The “yes” score within each domain was given only if the majority of items were fulfilled and indicated low risk of bias. Results of risk of bias assessment were summarized for each domain across studies. An overall risk of bias in each study (eg, summary score) was not provided in accordance with the current recommendations.²⁸

Data extraction and analysis

Data from included studies were extracted independently by two reviewers using a piloted standardized data extraction sheet. Data extracted included information about study design, sample size, study population (eg, participant demographics and LBP features), recruitment source, inception time, follow-up duration, prognostic variables analyzed,

outcome measures adopted, statistical analysis performed, and key findings. Any disagreement was resolved by discussion and consensus among the two reviewers.

Due to heterogeneity between studies with respect to LBP duration, clinical outcomes, follow-up duration, and statistical methods, it was not possible to statistically pool the results. Instead, findings were reported descriptively.

Results

The search strategy retrieved 8,628 articles from which 6,422 articles remained after duplicates were removed and 30 after screening by titles and abstracts. Full-text copies were then examined for eligibility (Figure 1). The reasons for exclusion at the full-text stage were: ineligible study design, QST assessment not performed, outcomes of LBP status at follow-up not reported, and ineligible participants. Three studies met the eligibility criteria and were therefore included.

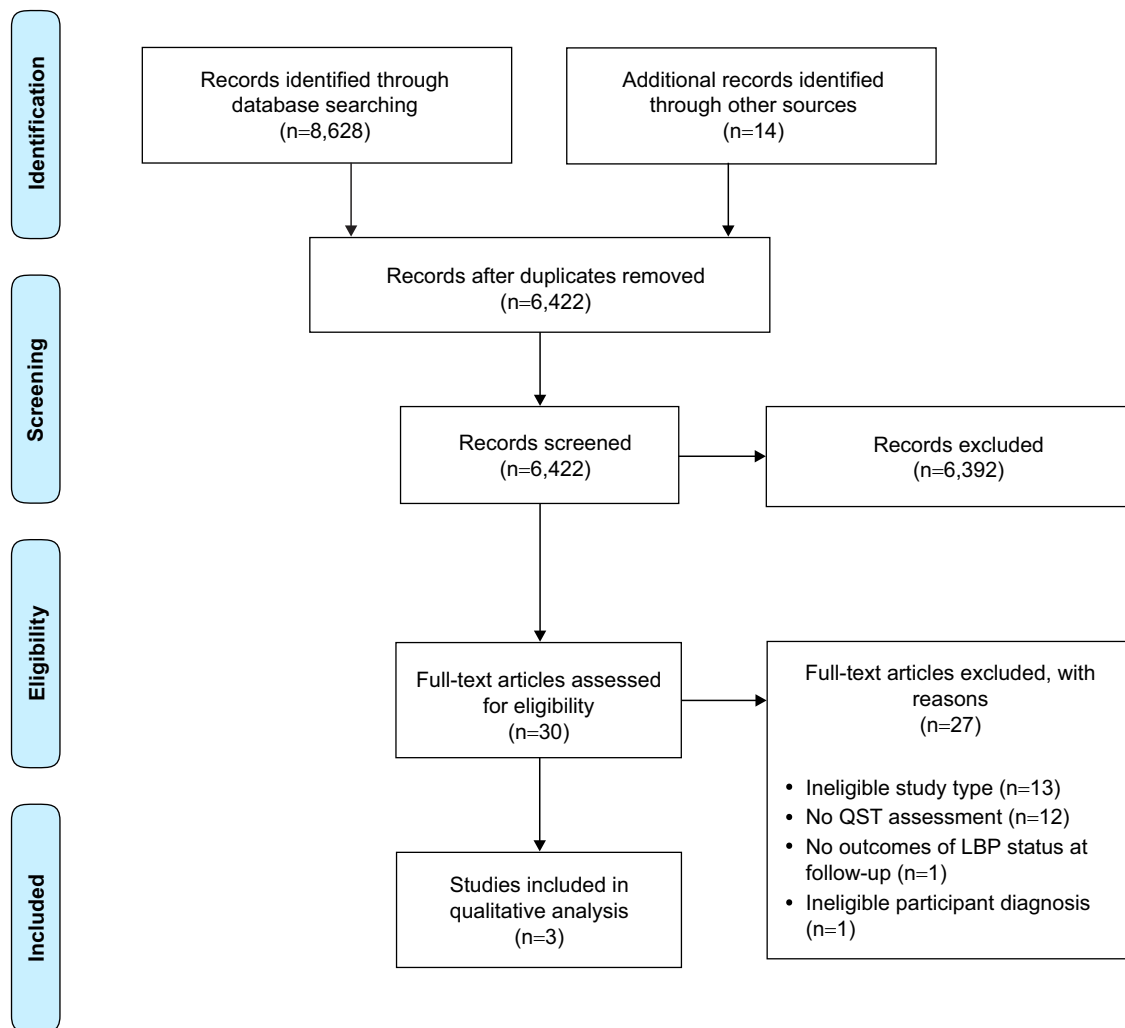


Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart. **Abbreviations:** LBP, low back pain; QST, quantitative sensory testing.

An additional 14 studies from the reference lists of included studies were screened, but none were eligible for inclusion. None of the experts in the field who were contacted by the review team had data that fulfilled our criteria or were able to provide results from current prospective studies.

Characteristics of samples in the included studies

A description of the samples from the included studies is provided in Table 1. Two studies recruited patients with LBP from primary care practices^{29,30} and one study from tertiary care.³¹ LeResche et al²⁹ assessed 157 patients who made their first visit for mechanical LBP to a primary care clinic of the Group Health in the Seattle area (USA) who were followed up at 4 months. In this cohort, 65% of patients had LBP for less than 4 weeks, while the remaining 35% had a longer, variable duration of LBP. Mlekusch et al³¹ recruited 113 patients with chronic LBP without radicular pain, from a University Pain Clinic in Bern (Switzerland) who were followed up at 12–15 months. The authors reported that some patients received predominantly interventional treatments (eg, steroid injections, neural therapy, radiofrequency, surgery, acupuncture, and electrothermal therapy) between baseline assessment and follow-up. Nordeman et al³⁰ investigated 113 females with

chronic LBP with or without leg pain identified through a search of medical records of eight primary health care clinics in Sweden, and were followed up for 2 years after baseline assessment.

Risk of bias assessment

Regarding the risk of bias evaluation (Table 2), three domains with high risk of bias were identified across the three included studies, which potentially compromise the validity of these results. These domains were as follows: the representativeness of samples, the reporting of QST assessment, and the adequacy of the outcome measure. However, all three studies satisfactorily described their samples, had low attrition bias (follow-up rates more than 90%), and reported statistical adjustment for relevant demographic or clinical/psychological factors.

Association of QST findings with clinical outcomes

All three studies investigated the association of pressure pain responses with LBP outcomes in univariate and multivariate analyses. LeResche et al²⁹ found a significant association between pressure pain threshold (PPT) at the back and at the thenar eminence of the hand, with clinically significant

Table 1 Characteristics of samples in the included studies

Characteristics	LeResche et al ²⁹	Mlekusch et al ³¹	Nordeman et al ³⁰
Geographical area	USA (Seattle)	Switzerland	Sweden
Setting	Primary care	Tertiary care	Primary care
Population under study	Acute LBP	Chronic LBP	Chronic LBP
Exclusion criteria for LBP	LBP due to neoplastic, infectious or inflammatory cause, pregnancy or major trauma	LBP with radicular pain confirmed by MRI finding of nerve compression together with symptoms or signs of nerve dysfunction	LBP due to pregnancy, known spinal disorders, or other severe disorders
Female, n (%)	157 ^a (61.8)	113 (57)	130 (100)
Mean age (SD), years	47.4 (12.4)	50.8 (15.4)	45 (10)
Mean pain duration (SD), years	LBP ≤30 days (in 65% of sample)	6.1 (6.4)	9.6 (8.8)
Follow-up duration	4 months	12 to 15 months	2 years
Loss to follow-up (%)	6	0	5
Events, n (%) ^b	44 (30)	N/A	27 (22)

Notes: ^aThe cohort was 571, but only 157 participated in the QST; ^bfor LeResche et al.²⁹ this is the number of people who had clinically significant pain at 4 months; for Nordeman et al.³⁰ this is the number of people who were in the “no work ability” category at 2 years.

Abbreviations: LBP, low back pain; SD, standard deviation; N/A, not applicable; MRI, magnetic resonance imaging; QST, quantitative sensory testing.

Table 2 Risk of bias assessment using the adapted version of the QUIPS tool

Reference	Sampling		Study attrition	Prognostic factors measurement	Outcome measurement	Study confounding	Statistical analysis and reporting
	Sample defined	Sample representative					
LeResche et al ²⁹	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes
Mlekusch et al ³¹	Yes	No	Yes	Yes	Yes	Yes	Yes
Nordeman et al ³⁰	Yes	Unclear	Yes	Unclear	Unclear	Yes	Yes

Abbreviation: QUIPS, Quality in Prognostic Studies.

pain intensity at 4 months (odds ratio [OR]: 0.66 [95% CI 0.44–0.96] and 0.62 [95% CI 0.40–0.92], respectively). However, this association was not significant when adjusted for age and sex in the multivariate model. In a study by Nordeman et al,³⁰ results from the univariate analysis revealed that people with chronic LBP with higher PPT – measured at eight tender points – were significantly more likely to be able to work at 2 years (OR: 1.4 [95% CI 1.1–1.9]). In the multivariate analysis, when age; functional status; psychological, environmental, and health-related factors; activity; and participation limitations were entered into the model as independent variables, PPT was no longer a significant independent predictor of work status at 2 years. However, reduced walking speed (measured by the 6-minute walk test), higher depression (measured by the Hospital Anxiety and Depression Scale-depression subscale), and previous inability to work remained in the final model, explaining 51% of the variance in the outcome at 2 years. Mlekusch et al³¹ found no association of pressure pain tolerance threshold measured at the toe with change in pain intensity at 12–15 months in people with chronic LBP, when controlling for baseline pain intensity ($r=0.03$ [95% CI –0.21–0.28]). When adjusted for demographics and psychological and clinical variables, the association remained nonsignificant ($r=-0.01$ [95% CI –0.28–0.27]).

The prognostic value of cold pressor testing was reported in two studies. In LeResche et al,²⁹ cold pain sensitivity was assessed as the average pain intensity at 10, 20, and 30 seconds after immersion of the hand in cold water at 4°C–5°C. In both the univariate and adjusted analyses, there was no significant association of cold pressor pain rating with clinically significant pain at 4 months (OR: 1.04 [95% CI 0.72–1.51] and 0.91 [95% CI 0.61–1.36], respectively). In Mlekusch et al,³¹ cold pain tolerance was measured as the time participants could tolerate immersion of their hand in cold water at 0°C (up to a maximum of 2 minutes). The association of cold pain tolerance with change in pain intensity at 12–15 months was near null in both the univariate ($r=-0.02$ [95% CI –0.23–0.28]) and adjusted analyses ($r=-0.00$ [95% CI –0.26–0.25]).

CPM was assessed in two studies,^{29,31} with noxious cold water as the conditioning stimulus in both studies. In LeResche et al,²⁹ heat pain was used as the test stimulus, measured before and again during immersion of the hand in cold water. In Mlekusch et al,³¹ pressure pain tolerance was used as the test stimulus measured before and again after removal of the hand from the cold water. The CPM response was measured as the difference between heat pain rating and pain threshold, before and after the conditioning stimulus. Both studies reported no association of the CPM response

with outcomes in the acute (OR: 1.11 [95% CI 0.77–1.62]) and chronic ($r=-0.40$ [95% CI –0.80–0.00]) LBP samples studied.

Finally, one study²⁹ assessed mechanical temporal summation using repeated application of a von Frey filament at the forearm. No significant association was observed between temporal summation and clinically significant pain at 4 months, in both the univariate (OR: 0.92 [95% CI 0.63–1.31]) and adjusted (OR: 0.88 [95% CI 0.58–1.27]) analyses. A summary of these results is presented in Table 3.

Discussion

This systematic review has revealed a surprising finding that there are very few studies which investigated the prognostic value of QST responses in people with LBP. In the three studies that were included in this review, none reported any significant association between the QST responses tested and LBP outcomes measured between 4 months and 2 years in both acute and chronic LBP.

Other studies have reported negative findings between QST responses and LBP outcomes. For example, in a systematic review of cross-sectional analyses, no correlation was found between QST responses and spinal pain and disability, regardless of the QST modality used, the site of assessment, or pain duration.³² The authors of the review noted this observed finding may be because pain thresholds (eg, pressure pain detection threshold) were predominantly assessed in the included studies, rather than suprathreshold or dynamic QST tests. In another example, O’Neill et al³³ investigated risk factors for LBP in the general population, and found that people with lower PPT (below the 10th percentile of PPT distribution) were not at higher risk of developing future LBP. Whether or not this result would have been different if suprathreshold measures of pain sensitivity were used is unknown. However, if indeed dynamic QST tests are more clinically relevant measures of pain sensitivity, then we would have expected an association in the studies reporting these measures in the current review. One explanation could be the low prevalence of pain hypersensitivity in the cohorts investigated. Indeed, one of the three studies³¹ in this review did report that only a small proportion of people (approximately 25%) with severe long-lasting LBP had QST responses below the 10th percentile of normative data distribution, indicative of widespread pain hypersensitivity. It remains unknown whether this may have been a factor in the other two studies as prevalence data regarding pain hypersensitivity were not available.

When prospective studies investigating other pain conditions were examined, there are examples where QST

Table 3 Summary of the main findings

Reference	Stimulus	Pain measure	Site	Other variables	Outcome measure	Statistical analysis	Results (univariate analyses)	Conclusions
LeResche et al ²⁹	Pressure	Pain threshold	Back and hand	Age Sex	Clinical significant pain measured by the Graded Chronic Pain Scale: “no” defined as grade 0 or I; “yes” defined as grade II, III, IV	Univariate and multivariable logistic regression	Only PPT at the back and PPT at the thenar eminence were significantly associated with clinically significant pain at 4 months ($P<0.5$)	None of the QST measures were significant predictors of clinical significant pain at 4 months after controlling for patient age and sex
	Cold	Pain magnitude rating	Hand					
	Mechanical	Temporal summation	Forearm					
	CPM	Cold bath (CS) and heat pain (TS)	Hand (CS) and forearm (TS)					
Mlekusch et al ³¹	Pressure	Pain tolerance	Toe	Pain severity and duration, age, sex, catastrophizing, depression, intake of opioids	Change score in average pain intensity over the last 24 hours measured by numeric rating scale (NRS11)	Univariate and multivariable linear regression	None of the QST variables showed an association with change score in pain severity at 1 year	None of the QST measures were significantly associated with change score in pain severity at 1 year in both the unadjusted and adjusted analyses
	Cold	Pain tolerance (time to withdrawal)	Hand					
	CPM	Cold bath (CS) and PPtol (TS)	Hand (CS) and toe (TS)					
Nordeman et al ³⁰	Pressure	Pain threshold	Trapezius, supraspinatus, gluteal, and knee bilaterally	Age, baseline work ability, walking test, hand grip strength, number of pain localizations, widespread pain, pain severity, fatigue, activity limitation, social support, risk of long-term disability, stress, anxiety, depression, general health status	Work ability: “no” defined as full-time sick leave or full-time disability pension; “yes” defined as work or study, applying for work, parental leave, or part-time disability pension	Univariate and forward stepwise logistic regression	PPT was significantly associated with work ability at 2 years ($P=0.018$)	Walking ability together with depression score and baseline work ability were significant predictors accounting for 51% of the variance in work ability at 2 years

Abbreviations: PPT, pressure pain threshold; CPM, conditioned pain modulation; PPtol, pressure pain tolerance; CS, conditioning stimulus; TS, test stimulus; QST, quantitative sensory testing.

responses do predict outcomes. For example, cold pain hypersensitivity and PPTs have been found to be of prognostic value in both whiplash-associated disorders^{11–13} and lateral epicondylalgia.¹⁴ Further, a recent systematic review showed that responses to psychophysical tests (ie, lower thermal, mechanical, and electrical pain tolerances or thresholds) explained up to 54% of the variance in postoperative pain following gynecological, orthopedic, and thoracotomy surgical procedures.³⁴ For example, cold pain tolerance measured preoperatively was identified as an independent risk factor for early postoperative pain in cholecystectomy.³⁵ While these studies in musculoskeletal and perioperative pain have shown

an association of QST findings with outcome, the overall number of prospective studies examining the predictive capacity of QST to identify those at greatest risk of persistent pain and poor functional outcomes remains small; therefore, further research is needed to confirm these results.

In the studies included in the present review, a number of methodological limitations that need to be taken into consideration when interpreting these findings were identified. The first concern was the “representativeness of the samples”. It is well established that the most useful prognostic studies are those which assemble an inception cohort,^{26,27} yet only survivor cohorts were recruited in the studies in this review.

For example, in two studies^{30,31} the participants had chronic LBP with a mean pain duration of 9.6 (standard deviation [SD] 8.8) years and 6.1 (SD 6.4) years. One study²⁹ attempted to assemble a LBP cohort of less than 30 days duration. However, 35% of the participants had duration longer than 30 days, and the pain duration details were not provided for this sample. Further, in Mlekusch et al,³¹ only patients seeking care to a pain clinic were included, which further limited the generalizability of these results.²⁶ The second methodological issue pertains to the “measurement of prognostic factors”. It was mostly unclear whether QST measures were performed in the same manner for all participants since information about the test protocol (eg, patient positioning, order of the tests, description of assessor training, number of assessors, and use of standardized instructions) as well as blinding of QST assessors were not reported. Standardized testing procedures ensure adequate reliability of QST measures.^{36,37} Poor reliability of QST measures can dilute or mask prognostic information.³⁸ The last methodological issue is the “adequacy of the outcome measures”. In Nordeman et al,³⁰ the validity of the applied work status categories is unclear (eg, part-time disability pension was classified as “able to work”). Moreover, the responsiveness of the work outcome used in this survivor cohort of chronic LBP was low, as illustrated by the low change (1%) in people’s ability to work from baseline to 2 years.

Strengths and limitations

The strengths of this systematic review were that the research question was well defined with respect to the study design, population of interest, prognostic variables, and outcomes, and a thorough search strategy was used to identify all possible studies including unpublished data. The main limitations were that only a small number of studies met the inclusion criteria and they were heterogeneous with regard to LBP duration, clinical outcomes, follow-up duration, and statistical methods, which precluded quantitative analysis. In addition, the studies only assessed a limited range of QST measures, namely, mechanical and cold pain threshold and tolerance, temporal summation, and CPM. Therefore, it is not known whether other test modalities alone or in combination may have prognostic value in LBP. Additionally, the risk of bias issues discussed earlier further limit the generalizability of the findings.

Future perspectives

Future studies that aim to investigate the prognostic value of QST measures should focus on an inception cohort design,

employ multiple QST modalities that are comprehensively described, and use standardized protocols, blinded assessors, and validated and appropriate outcome measures. Additionally, it would be valuable to concurrently assess known clinical and psychosocial predictors to account for the complexity and heterogeneity of LBP.

Conclusion

Due to the paucity of prospective cohort studies and the methodological shortcomings of available studies, it remains unknown whether QST measures are predictive of outcome in LBP. Given the developing body of literature suggesting QST as prognostic value for pain and function in various pain conditions, future prospective prognostic outcome studies of QST in LBP would be worthwhile.

Disclosure

The authors report no conflicts of interest in this work.

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Supplementary material

Table S1 Ovid Medline search

1. exp cohort studies/	39. hyp?esthesia.ti,ab.
2. incidence/	40. peripheral sensit*.ti,ab.
3. follow up stud*.mp.	41. central sensit*.ti,ab.
4. prognos*.mp.	42. spinal sensit*.ti,ab.
5. predict*.mp.	43. central pain.ti,ab.
6. course.mp.	44. (quantitative sensory test* or QST).mp.
7. inception.mp.	45. experim* pain.mp.
8. exp survival analysis/	46. ((pain adj test*) or (pain adj measure*)).mp.
9. exp risk/	47. bedside exam*.mp.
10. observational study/	48. psychophysic*.mp.
11. longitudinal studies/	49. Electrophysiologic*.mp.
12. or/1-11	50. (temporal summation or windup or wind up).mp.
13. back pain/	51. (second* adj pain).ti,ab.
14. low back pain/	52. (two-point discrimination or TPD).mp.
15. back disorder*.mp.	53. tactile acuity.ti,ab.
16. (lumbar adj pain).ti,ab.	54. (cold pressor test or CPT).mp.
17. sciatica/	55. (diffuse noxious inhibitory control or DNIC).mp.
18. sciatic neuropathy/	56. (pain modul* or descending modul*).mp.
19. Intervertebral Disc Degeneration/	57. (conditioned pain modulation or CPM).mp.
20. (dis* adj l prolapse*).ti,ab.	58. offset analgesia.mp.
21. (dis* adj l herniat*).ti,ab.	59. neural inhibition/
22. (facet adj joint*).ti,ab.	60. (nociceptive withdrawal reflex or NWR or nociceptive flexion reflex or NFR).mp.
23. backache.ti,ab.	61. (reflex receptive field or RRF).mp.
24. dorsalgia.mp.	62. (spinal reflex* or (Rill adj reflex)).mp.
25. or/13-24	63. pain threshold/
26. exp Pain Perception/	64. Nociceptors/
27. pain, referred/	65. ((pressure or thermal or cold or heat or electrical or mechanical) adj pain).ti,ab. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
28. allodynia.ti,ab.	66. ((cold or warm) adj detection).ti,ab.
29. neuralgia/	67. ((pain adj2 tolerance) or (pain adj2 processing) or detection threshold).ti,ab.
30. hypersensit*.mp.	68. or/26-67
31. hyperpathia.ti,ab.	69. 12 and 25 and 68
32. exp somatosensory disorders/	70. 69 not randomized controlled trial/
33. sensory profile*.mp.	
34. hyp?algesia.ti,ab.	
35. hyperalg?esia.ti,ab.	
36. paresth?esia.ti,ab.	
37. hyperesth?esia.ti,ab.	
38. dysesth?esia.ti,ab.	

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