# Prevalence, characteristics and clinical course of neuropathic pain in primary care patients consulting with low back-related leg pain

Sarah A. Harrisson PhD\* a, c, Reuben Ogollah PhD b, Kate M. Dunn PhD a, Nadine E. Foster PhD a, Kika Konstantinou PhD a, c.

a Primary Care Centre Versus Arthritis, School of Primary, Community and Social Care, Keele University, Staffordshire, ST5 5BG, UK.

b Nottingham Clinical Trials Unit, University of Nottingham, Nottingham, NG7 2NR, UK.

c Haywood Hospital, Midlands Partnership Foundation Trust, Staffordshire, UK, ST6 7AG, UK.

\*Corresponding author:

Sarah Harrisson. Primary Care Centre Versus Arthritis, Research Institute for Primary Care and Health Sciences, Keele University, Staffordshire, ST5 5BG, UK.

Tel 01782 734928. Fax 01782 734719. s.a.harrisson@keele.ac.uk.

Category for which this manuscript is being submitted: Clinical Investigation

Conflict of Interest and Source of Funding:

The authors declare that they have no competing interests.

During the period in which this work was undertaken Sarah A. Harrisson was supported by a National Institute for Health Research (NIHR) Clinical Doctoral Fellowship funded through an NIHR Research Professorship for Nadine E. Foster (NIHR-RP-011-015). Nadine Foster is also a Senior NIHR Investigator. Kika Konstantinou was supported by a Higher Education Funding Council for England/ National Institute for Health Research Senior Clinical Lectureship. The views expressed in this publication are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care. This work also relates to an Education and Continued Professional Development (level 2) award by the Musculoskeletal Association of Chartered Physiotherapists (MACP) and a Travel Fellowship awarded by the Society of Back Pain Research to Sarah A. Harrisson in 2016.

Abstract

Objectives

Little is known about the epidemiology of neuropathic pain in primary care patients consulting with low back-related leg pain. We aimed to describe prevalence, characteristics and clinical course of low back-related leg pain patients with and without neuropathic pain, consulting with their family doctor in the UK.

Methods

This was a prospective cohort study. Data were collected using a standardised baseline clinical examination and self-report questionnaires at baseline, 4, 12 and 36-months.

We identified cases of neuropathic pain using three definitions: two based on clinical diagnosis (sciatica, with and without evidence of nerve root compression on MRI), one on the self-report version of Leeds Assessment for Neurological Symptoms and Signs (S-LANSS).

Differences between patients with and without neuropathic pain were analysed comparing each definition. Clinical course (mean pain intensity measured as the highest of leg or back pain intensity: mean of three Numerical Rating Scales, each 0-10) was investigated using linear mixed models over 36-months.

Results

Prevalence of neuropathic pain varied from 48% to 74% according to definition used. At baseline, patients with neuropathic pain had more severe leg pain intensity, lower pain self-efficacy, more patients had sensory loss than those without. Distinct profiles were apparent depending on neuropathic pain definition. Mean pain intensity reduced after 4-months (6.1 to 3.9 (sciatica)), most rapidly in cases defined by clinical diagnosis.

Discussion

This research provides new information on the clinical course of neuropathic pain and a better understanding of neuropathic pain in low back-related leg pain patients consulting in primary care.

Key words

Low back pain; leg pain; primary care; neuropathic pain; epidemiology

## Introduction

Neuropathic pain, defined as pain caused by injury or disease of the somatosensory system,1 is considered to be challenging to manage. The symptoms of neuropathic pain, which may include feelings of burning, electric-shock and/or prickling,2 can be very distressing for patients. There is no gold standard for defining cases of neuropathic pain but there is some consensus for a hierarchical grading system to assist researchers and clinicians to identify cases of neuropathic pain.1 Patients with a pain condition, plausible clinical history and with relevant findings from neurological examination meet the criteria for having ‘possible’ neuropathic pain. With the addition of appropriate findings from diagnostic tests, patients meet the criteria for having ‘probable’ neuropathic pain. The majority of patients with neuropathic pain are managed in primary care,3 even if consulting with severe and bothersome pain. In primary care, where clinicians are non-specialists, neuropathic pain screening tools (for example self-report version of Leeds Assessment of Neuropathic Symptoms and Signs (s-LANSS)4 have been suggested as useful to identify patients with possible neuropathic pain.5

Low back pain (LBP) is thought to be one of the most common neuropathic pain presentations6 and is the leading cause of disability globally.7 Leg pain related to back pain (LBLP) is one of the most common presentations of LBP8,9 and is associated with increased pain, disability and poorer quality of life compared to LBP alone.10 For this reason there is an argument that LBLP patients should be considered as distinct for research purposes from those with LBP.11 LBLP is clinically diagnosed as having sciatica (also termed lumbar spinal nerve root pain or radicular pain) or referred leg pain, where sciatica is thought to be neuropathic12 and referred leg pain to be nociceptive.

There are specific pharmacological and non-pharmacological treatments (physiotherapy, cognitive behavioural therapy) available to LBLP patients with and without neuropathic pain in primary care. Guidelines advocate that neuropathic pain medications are considered for patients with sciatica.13,14 A diagnostic approach is important when it enables the provision of timely and targeted interventions as in acute illnesses, it is not clear whether this approach is useful for LBLP patients consulting in primary care. For many LBLP patients consulting in primary care, identifying neuropathic pain does not provide sufficient knowledge or evidence of likely future health outcomes.15 It is widely thought that LBLP patients with neuropathic pain do worse over time compared to those without, but evidence from a recent systematic review16 highlighted the paucity of evidence describing the prognosis of LBLP patients with neuropathic pain consulting in primary care.

The aims of this study were to describe: i) prevalence of neuropathic pain in LBLP patients consulting in primary care; ii) characteristics of LBLP patients with neuropathic pain; iii) the clinical course of LBLP patients with neuropathic pain at baseline in terms of pain intensity over short, intermediate and long-term time-points. Given there is no perfect standard for identifying cases of neuropathic pain, we provide and compare data on prevalence, characteristics and clinical course, by describing cases using clinical definitions for neuropathic pain and also a neuropathic pain screening tool.

## Materials and Methods

### Study design and patient recruitment

This is secondary analysis of a prospective, multi-centre cohort study, the Assessment and Treatment of Leg pain Associated with the Spine (ATLAS) study, of LBLP patients consulting and receiving treatment in primary care. Ethical approval was granted by the South Birmingham Research Ethics Committee (REC ref 10/H1207/82) in October 2010 for the original study, and by NRES Committees North of Scotland (REC Ref. 13/NS/0170) for the longer-term follow-up. All analyses in this report were nested within this programme of work. Adults aged 18 years and over with LBLP of any duration and severity, who consulted with their family doctor, were invited to take part in the ATLAS study. For the full details of the recruitment procedure see the ATLAS study protocol,17 the flow of patients in the ATLAS study is summarised in Figure 1. Patients were considered to have LBLP if they presented with leg pain that spread from the lower back beyond the gluteal fold to anywhere in the leg. Pain was considered to include unpleasant sensations such as pins and needles or numbness. Patients were excluded if there was suspected serious spinal pathology, previous spinal surgery, pregnancy, they were receiving physiotherapy treatment (or osteopathy or chiropractic) or were under the care of a specialist consultant in secondary care for the same condition, those with serious physical or mental co-morbidity that would prevent them attending the research clinic or undergoing the study’s procedures, or inability to read and speak English.

All participants in the study were assessed by physiotherapists and a neurological examination was carried out as part of the clinical examination as recommended in LBP guidelines19 and specialist books (for example, Examination of the Lumbar Region in Neuromusculoskeletal Examination and Assessment, pages 329 to 330).20 At the time of the clinical examination, a clinical diagnosis of either sciatica or referred leg pain was made. In this research, a clinical diagnosis of sciatica was characterised by leg pain that may radiate to beyond the knee and into the foot or toes, and may be accompanied by muscle weakness and/or reflex change and/or pins and needles or numbness (paraesthesia), in a specific nerve root(s) distribution.21 The term sciatica is indicative of nerve root compression causing radicular pain with or without neurological deficits and the criteria for clinical diagnosis was pre-determined following consensus from a Delphi study.22

All physiotherapists in the ATLAS study were given training in the study’s procedures. There was fair agreement between physiotherapists in this study when making a diagnosis of sciatica or referred leg pain. The full details of the agreement and reliability amongst the clinicians in the ATLAS study when diagnosing low back-related leg pain are provided elsewhere.23 All patients in the ATLAS study were invited for a magnetic resonance imaging (MRI) scan within ten days of attending their assessment at the ATLAS research clinic, except in cases where this imaging was contraindicated, or when the patient did not wish to have a scan, or when an MRI scan was already available in the previous 6-months for the same clinical presentation. Data used in this analysis were collected at baseline and at three follow-up points at 4-months, 12-months and 3-years using postal self-complete questionnaires.

### Treatment pathways

Treatment plans for patients in the study were agreed between the treating physiotherapist and the patient, and according to current best clinical evidence and practice guidelines. For those patients where physiotherapy management was indicated, up to six (on average) treatment sessions (of 30 minutes) were delivered over six to eight weeks. If a patient’s symptoms worsened or failed to improve, pathways were in place so that appropriate referrals could be made to specialist spinal services for further assessment and management including onward referral to spinal surgeons and pain specialists.

### Selected characteristics of interest

The characteristics chosen to describe LBLP patients with and without neuropathic pain were based on sociodemographic information (age, sex, socioeconomic status based on type of work, smoking status and body mass index (BMI)), health status (presence of diabetes, general health24, fatigue and sleep difficulties), information about pain (mean back pain intensity, mean leg pain intensity,25 pain described as burning, duration of pain, pain location, presence of widespread pain), limitations in activities (back and leg pain related disability using the Roland and Morris Disability Questionnaire (RMDQ)26 leg version,27 psychological variables (symptoms of depression and anxiety using the Hospital Anxiety and Depression Scale (HADS) 28), pain self-efficacy beliefs using the Pain Self-Efficacy Questionnaire (PSEQ),29 findings from neurological examination (presence of muscle weakness, tendon reflex, sensation to pin prick, presence of pins and needles, pain affecting the colour of patients skin, presence of allodynia or hyperalgesia in the leg(s), neural tension test and imaging using MRI), and the number of pain medications used. See Table S1, Supplemental Digital Content, for full details of all the characteristics collected in this study.

### Data Analysis

Cases of neuropathic pain were identified using three definitions of neuropathic pain: two based on clinical diagnosis (sciatica21, 22 with and without evidence of nerve root compression on MRI), one on the self-report using s-LANSS4 (see Table 1. for a detailed description of each of the three definitions of neuropathic pain used in this research). Prevalence was estimated for three definitions of neuropathic pain. Descriptive statistics (mean and standard deviation (SD) for continuous variables and frequency and percentage for categorical variables) were used to describe characteristics of interest in those with neuropathic pain for each of the neuropathic pain definitions. Logistic regression was used to examine the association between neuropathic pain (based on the three definitions), characteristics of interest and was based on the analysis of complete cases.

For describing the clinical course, linear mixed models, with a neuropathic pain indicator variable (according to neuropathic pain definition used) by time interaction, were used to estimate the unadjusted mean and 95% confidence intervals (CI) of pain intensity at all three follow-up time-points. CIs were obtained to evaluate the uncertainty of estimates taking into account the missing data.30 Margins plots were used to graphically summarise the information on the clinical course.

All statistical analyses were performed using Stata version 14.0.31 The STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) checklist for cohort studies was used when writing the report.32

### Measures of clinical course

Pain intensity scores at baseline, 4-months, 12-months and 3-years, were used to describe the clinical course of this patient population. Pain intensity was determined as the highest of mean leg pain intensity or mean back pain intensity in the previous two weeks, where leg pain intensity was determined as the mean of three 0-10 NRS for current, usual and least leg pain over the previous two weeks, and back pain intensity as the mean of current, usual and least back pain over the previous two weeks.25

## Results

### Study population

In total, 609 patients with LBLP were eligible and consented to participate in the study; patients received a clinical diagnosis of either referred leg pain or sciatica and 554 had an MRI. Three out of 609 patients did not complete all seven items of the s-LANSS. In total, 402 (66.0%) completed the study questionnaire at 4-months, 450 (73.9%) at 12-months, and 316 (51.9%) at 3-years. Patients who responded to follow-up at 4-months were older than non-responders (mean 54 years compared to 42 years), fewer scored 12 or greater on s-LANSS (45% compared to 55%), a slightly higher proportion had a clinical diagnosis of sciatica (77% compared to 70%) and they had slightly lower LBLP-related disability (mean RMDQ 12.1 compared to 13.7) at baseline. This was consistent at 12-months and 3-years. Nearly nine out of ten (88.0%) patients in the ATLAS cohort received a course of physiotherapy treatment and 11.4% of patients were referred to specialist services for further treatment or investigations. A slightly higher proportion (14.3%) of patients with neuropathic pain based on a clinical diagnosis of sciatica with evidence NRC were referred for an epidural injection or to spinal surgeons. Table S2 (Supplemental Digital Content) gives details on the care provided to patients in the ATLAS study according to the three definitions of neuropathic pain.

### Prevalence of neuropathic pain in LBLP patients

The prevalence of neuropathic pain was 74.2% based on a clinical diagnosis of sciatica (452 out of 609), 48.8% based on s-LANSS (296 out of 606), and 45.5% based on sciatica with evidence of possible or clear NRC (252 out of 554). Just under one quarter (23.0%, 127 out of 551) of LBLP patients were defined as having neuropathic pain using all three definitions. Nearly four in ten patients (38.3%, 232 out of 606) were defined as having neuropathic pain based on s-LANSS and clinical diagnosis of sciatica. Around one in ten (10.7%, 61 out of 606) were defined as having neuropathic pain based on s-LANSS, but were not by clinical diagnosis of sciatica either with or without evidence of NRC. The distributions and overlap of LBLP patients with or without neuropathic pain, based on the three definitions, are summarised in Figure 2.

### Characteristics of LBLP patients with neuropathic pain.

The profile of patients with neuropathic pain based on s-LANSS was quite distinct compared

to those without; they were more often current smokers, presented with more severe back pain intensity, more scored higher for depression and anxiety, more had an increased response to either non-painful or painful stimuli on clinical examination and more often used two or more pain medications compared to those without neuropathic pain. The profile of patients with neuropathic LBLP based on s-LANSS was also quite distinct compared to those with neuropathic pain based on clinical diagnosis of sciatica either with or without evidence of NRC on MRI. There were few differences in terms of health status, limitations in activities, psychological variables and pain medication use between patients with neuropathic pain based on clinical diagnosis of sciatica compared to those more stringently defined as having a clinical diagnosis of sciatica with evidence of NRC based on MRI.

The characteristics of LBLP patients with and without neuropathic pain based on s-LANSS, those with neuropathic pain based on a clinical diagnosis of sciatica, and those with LBLP based on clinical diagnosis of sciatica plus evidence of possible or clear NRC on MRI, respectively are provided in Tables 2, 3 and 4. LBLP patients with neuropathic pain, across all three neuropathic pain definitions, reported more severe leg pain (for a one-unit increase in NRS score for leg pain intensity, the odds (95% CI) presenting with neuropathic pain based on s-LANSS increased by 1.20 (1.12, 1.29), the odds of having a clinical diagnosis of sciatica increased by 1.32 (1.21, 1.44) and the odds of having a clinical diagnosis of sciatica plus evidence of NRC based on MRI increased by 1.29 (1.19, 1.40)); patients with pain below the knee were more likely to present with neuropathic pain compared to those without with the odds ratios (95% CI) of 1.98 (1.38, 2.87), 9.03(6.00, 13.60), and 4.18 (2.74, 6.37) for definition based on s-LANSS, clinical diagnosis of sciatica and clinical diagnosis of sciatica plus evidence of NRC based on MRI, respectively; and more had a weaker belief in the ability to cope with normal activities despite the pain (pain self-efficacy) compared to those without (for a one unit decrease in PSEQ score, the odds of presenting with neuropathic pain based on s-LANSS increased by 0.97 (0.97, 0.98), by 0.98 (0.98, 0.997) for those with a clinical diagnosis of sciatica and by 0.98 (0.97, 0.99) for those with a clinical diagnosis of sciatica plus evidence of NRC based on MRI).

Based on findings from neurological examination and consistently across all three definitions of neuropathic pain, patients with a reduction in sensation to pin-prick were more likely to present with neuropathic pain (odds ratios (95% CI) 1.64 (1.16 to 2.33), 3.87 (2.43, 6.16), 1.76 (1.22, 2.54) for definition based on s-LANSS, clinical diagnosis of sciatica and clinical diagnosis of sciatica plus evidence of NRC based on MRI, respectively) and those with a significant reduction or absence of tendon reflex (odds ratios (95% CI) 1.68 (1.06, 2.65), 4.42 (2.09, 9.38), 5.63 (3.22, 9.86) for definition based on s-LANSS, clinical diagnosis of sciatica and clinical diagnosis of sciatica plus evidence of NRC based on MRI, respectively) were more likely to present with neuropathic pain compared to those without. The presence of mild muscle weakness (myotomal) was found in 100% of patients with a clinical diagnosis of sciatica with or without evidence of NRC on MRI, and was associated with those patients with neuropathic pain based on s-LANSS.

### Clinical course

Pain intensity decreased over time and most of the change occurred between baseline and 4-months, irrespective of the neuropathic pain case definition used. Mean pain intensity in patients with neuropathic pain at baseline (across the three definitions) ranged from 6.1 to 6.3, decreasing to between 3.8 and 4.3 at 4-months (see Figures 3a-3c). Improvement in pain intensity plateaued around 4-months and changed very little up to 36-months for all neuropathic pain definitions (mean pain intensity of patients with neuropathic pain at 3-years ranged from 3.3 to 3.9 for the three definitions).

Patients with neuropathic pain (based on s-LANSS) had higher mean pain intensity (95% CI) compared to those without at 12-months (4.4 (4.1, 4.7) vs 3.0 (2.7, 3.3)), but not at 3-years (3.9 (3.5, 4.3) vs 3.0 (2.7, 3.4)). Patients with neuropathic pain (based on a clinical diagnosis of sciatica) had lower mean pain intensity compared to those without at twelve months (3.6 (3.3, 3.8) vs 4.0 (3.5, 4.4)) and at 3-years (3.3 (3.1, 3.6) vs 3.8 (4.4, 4.3)). Those patients with sciatica plus MRI evidence of NRC had lower mean pain intensity at 4-months (3.8 (3.5, 4.2) vs 4.1 (3.8, 4.3)), 12-months (3.3 (3.0, 3.7) vs 4.0 (3.7, 4.4)) and 3-years (3.3 (3.9, 3.6) vs 3.6 (3.2, 4.0)).

## Discussion

This is the first prospective cohort including LBLP patients consulting in primary care with neuropathic pain, and the first time that data on the clinical course of neuropathic LBLP over short, intermediate and long-term time-points, has been reported. Prevalence estimates of neuropathic pain in this patient population varied from 48% to 74% depending on the neuropathic pain definition used. Irrespective of case definition, our study shows that the presence of neuropathic pain in LBLP patients consulting in primary care, is common. LBLP patients with neuropathic pain based on s-LANSS presented with a more severe profile overall compared to those with neuropathic pain based on a clinical diagnosis of sciatica with or without MRI evidence of NRC. We found several characteristics that were common across the three definitions of neuropathic pain; higher leg pain intensity, lower pain self-efficacy, higher proportion of patients with pain below the knee, sensory deficits in the painful leg, mild muscle weakness (myotomal) and reduction in reflex. On average, there was early improvement in the clinical course in terms of pain intensity reduction followed by a plateau, with clinical course being worse only for those patients with neuropathic pain identified using the s-LANSS compared to those without.

Many patients with neuropathic pain defined by a diagnosis of sciatica were not identified as having neuropathic pain based on s-LANSS. This finding is consistent with previous literature reporting that many patients with neuropathic pain based on a clinical diagnosis of sciatica were not identified as having neuropathic pain based on neuropathic pain screening tools such as PainDETECT and DN4.16,33 Screening tools such as s-LANSS which are completed by self-report and where higher scores indicate the possible presence of neuropathic pain, may not be representative of underlying neuropathic mechanisms specifically, in these patients with sciatica.

This research provides the highest quality evidence to date on the characteristics of this patient population. As expected, the characteristics of patients with neuropathic pain varied depending on the method used to define cases. Patients with neuropathic pain based on s-LANSS presented with a distinctly different profile compared to those with neuropathic pain based on clinical diagnosis of sciatica. Depression, anxiety and use of two or more pain medications were more common in patients with neuropathic pain based on s-LANSS compared to those with neuropathic pain based on clinical diagnosis of sciatica with or without MRI evidence of NRC. This is consistent with previous research of patients with and without neuropathic pain based on clinical examination,33-35 which found fewer differences in pain duration, LBLP-related disability, depression, anxiety, and health-related quality of life between patients with and without neuropathic pain compared to those research studies using screening tools to identify cases of neuropathic pain.36-38 None of the previous studies33-38 aimed to describe the characteristics of LBLP patients with or without neuropathic pain and, in part, were limited by either small sample sizes or poorly defined comparator groups.

The clinical course of patients with and without neuropathic pain at baseline, in terms of pain intensity, showed some consistent similarities across the three neuropathic pain definitions used. On average, most improvement in pain intensity occurred between baseline and 4-months, followed by a plateau through to 3-years. This pattern of mean improvement is similar to the clinical course of LBP patients39 and patients with other musculoskeletal pain conditions.40

One of the assumptions underpinning this research is that the prognosis of patients with neuropathic pain is considered to be worse compared to those without. The clinical course of patients with neuropathic pain based on s-LANSS was worse than those without 12-months after initially consulting in primary care with LBLP, but this was not the case for the two other definitions of neuropathic pain. The finding that the clinical course is worse in patients with s-LANSS ≥ 12 is consistent with previous research using PainDETECT to define neuropathic pain cases36. We did not find that patients with “probable” neuropathic pain (those patients with a clinical diagnosis of sciatica with MRI evidence of NRC) has a worse clinical course than those with “possible” neuropathic pain (those more broadly defined by the clinical diagnosis of sciatica without MRI evidence of NRC). Our study shows that it is not the presence of neuropathic pain *per se* that is associated with poor prognosis, but specifically the presence of self-reported neuropathic pain.

In patients with a clinical diagnosis of sciatica (with or without evidence of NRC), the clinical course seemed more favourable compared to those without (i.e. those with a diagnosis of referred leg pain). There was some evidence that a higher proportion of patients with a clinical diagnosis of sciatica (with evidence of NRC) may have received more targeted care (for example epidural injection) compared to those without and compared to those with neuropathic pain based on s-LANSS. The absolute difference in the numbers receiving more targeted care across the three definitions was low and the differences in pain intensity between patients with and without neuropathic pain based on a clinical diagnosis of sciatica (with or without evidence of NRC) were often small with no obvious clinical relevance. This provides confidence that the course of patients with sciatica (either with or without evidence of NRC) was not confounded by treatment in this cohort and is similar to those without.

The strengths of this research include: i) the collection of a broad range of self-report data and clinical assessment findings from standardised clinical examinations including MRI scans; ii) the long-term prospective cohort study design allowed for investigation of the temporal relationship between neuropathic pain at baseline and pain intensity over 3-years, this addresses the limitations of previous research with this patient population,41 and; iii) the use of mixed-effect models for repeated measures which take into account fixed effects (presence or absence of neuropathic pain at baseline), random effects (individual patients), interaction between time and the outcome (pain intensity) and missing data (using likelihood-based approaches) during model development.

### Limitations

Given that a number of characteristics were found to be very strongly associated with neuropathic pain (e.g. neurological examination findings were strongly associated with a clinical diagnosis of sciatica; self-report of burning pain was strongly associated with neuropathic pain based on s-LANSS), there is a risk of bias due to the incorporation of characteristics that were used to determine cases of neuropathic pain. Incorporation bias can lead to an overestimation of the strength of an association between a characteristic and an outcome, in this research neuropathic pain being the outcome42 However, using three accepted neuropathic pain case definitions, and comparing the characteristics of patients with neuropathic pain using each definition, adds confidence about the characteristics of these patients. Despite some evidence of incorporation bias, overall there seems to be limited impact on the main findings of the study.

### Implications for clinical practice and research

The implication of using different methods to identify cases of neuropathic pain is inevitably variation in prevalence estimates, characteristics and clinical course; it is not clear what the implication is in terms of variation in response to treatment. Given the few differences between patients with sciatica with or without evidence of NRC on MRI, both at baseline and in terms of clinical course over 3-years, the clinical implication of our study is that in the absence of widespread or progressive neurological deficit, most LBLP patients with a clinical diagnosis of sciatica (with or without evidence of NRC) should be treated, at least initially, conservatively. Imaging should be reserved for those patients for whom the result is likely to change clinical management. In this research, patients with neuropathic pain based on s-LANSS had, on average, a more severe phenotype compared to those with neuropathic pain based on clinical diagnosis, however it is not known if routine use of s-LANSS in clinical practice would benefit patients. Our study provides empirical evidence that questions the usefulness of the hierarchical grading system1 to classify cases of neuropathic LBLP by clinical examination. Future epidemiological research is needed to investigate whether characteristics identified from self-report and routine neurological examination that are thought to be important for defining cases of neuropathic LBLP can predict a poor outcome in patients with self-reported signs and symptoms of neuropathic pain who do worse over time.

### Conclusions

Neuropathic pain in LBLP patients consulting in primary care is common, with a prevalence between 48% and 74% depending on the neuropathic pain case definition. Many patients with sciatica did not have neuropathic pain based on s-LANSS, suggesting that sciatica is not always a neuropathic pain condition. Prevalence and characteristics varied depending on the method used to define neuropathic pain. At baseline, LBLP-related morbidities such as depression, anxiety and worse general health were more common in patients with neuropathic pain based on s-LANSS compared to those with neuropathic pain based on clinical diagnosis of sciatica. Evidence of NRC from MRI increased the certainty of neuropathic pain but the prognosis of sciatica patients with or without NRC on MRI, was similar. The extent of the improvement in patients with neuropathic pain depended on the definition of neuropathic pain, only the clinical course of LBLP patients neuropathic pain defined using s-LANSS seemed to be worse compared to those without. This study challenges the commonly held assumptions that the clinical course of neuropathic pain is mostly poor.

## References

1. Treede RD, Jensen TS, Campbell JN, et al. Neuropathic pain: redefinition and a grading system for clinical and research purposes. *Neurology*. 2008;70(18):1630‐1635. doi:10.1212/01.wnl.0000282763.29778.59

2. Baron R, Binder A, Wasner G. Neuropathic pain: diagnosis, pathophysiological mechanisms, and treatment. *Lancet Neurol*. 2010;9(8):807‐819. doi:10.1016/S1474-4422(10)70143-5

3. Breivik H, Collett B, Ventafridda V, et al. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. *Eur J Pain*. 2006;10(4):287‐333. doi:10.1016/j.ejpain.2005.06.009

4. Bennett MI, Smith BH, Torrance N, et al. The S-LANSS score for identifying pain of predominantly neuropathic origin: validation for use in clinical and postal research. *J Pain*. 2005;6(3):149‐158. doi:10.1016/j.jpain.2004.11.007

5. Smith BH, Torrance N, Ferguson JA, Bennett MI, Serpell MG, Dunn KM. Towards a definition of refractory neuropathic pain for epidemiological research. An international Delphi survey of experts. *BMC Neurol*. 2012;12:29. doi:10.1186/1471-2377-12-29

6. Berger A, Sadosky A, Dukes E, et al. Clinical characteristics and patterns of healthcare utilization in patients with painful neuropathic disorders in UK general practice: a retrospective cohort study. *BMC Neurol*. 2012;12:8. Published 2012 Mar 6. doi:10.1186/1471-2377-12-8

7. Hoy D, March L, Brooks P, et al. The global burden of low back pain: estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis*. 2014;73(6):968‐974. doi:10.1136/annrheumdis-2013-204428

8. Hill JC, Konstantinou K, Egbewale BE, et al. Clinical outcomes among low back pain consulters with referred leg pain in primary care [published correction appears in *Spine* (Phila Pa 1976). 2012 Nov 15;37(24):E1541]. Spine (Phila Pa 1976). 2011;36(25):2168‐2175. doi:10.1097/BRS.0b013e31820712bb

9. Kongsted A, Kent P, Albert H, et al. Patients with low back pain differ from those who also have leg pain or signs of nerve root involvement - a cross-sectional study. *BMC Musculoskelet Disord*. 2012;13:236. Published 2012 Nov 28. doi:10.1186/1471-2474-13-236

10. Konstantinou K, Hider SL, Jordan JL, et al. The impact of low back-related leg pain on outcomes as compared with low back pain alone: a systematic review of the literature. Clin J Pain. 2013;29(7):644‐654. doi:10.1097/AJP.0b013e31826f9a52

11. Coggon D, Ntani G, Walker-Bone K, et al. Epidemiological Differences Between Localized and Nonlocalized Low Back Pain. Spine (Phila Pa 1976). 2017;42(10):740‐747. doi:10.1097/BRS.0000000000001956

12. Scholz J, Finnerup NB, Attal N, et al. The IASP classification of chronic pain for ICD-11: chronic neuropathic pain. *Pain*. 2019;160(1):53‐59. doi:10.1097/j.pain.0000000000001365

13. Finnerup NB, Attal N, Haroutounian S, et al. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. *Lancet Neurol* 2015;14:162-173. [http://dx.doi.org/10.1016/s1474-4422(14)70251-0](http://dx.doi.org/10.1016/s1474-4422%2814%2970251-0)

 14. National Institute for Health and Care Excellence. Neuropathic pain in adults: pharmacological management in non-specialist settings*.* NICE guideline CG173 2013. Retrieved from <http://nice.org.uk/guidance/cg173>. Last accessed 3 June 2019.

15. Croft P, Dinant GJ, Coventry P, et al. Looking to the future: should 'prognosis' be heard as often as 'diagnosis' in medical education?. *Educ Prim Care*. 2015;26(6):367–371. doi:10.1080/14739879.2015.1101863

16. Harrisson SA, Stynes S, Dunn KM, et al. Neuropathic Pain in Low Back-Related Leg Pain Patients: What Is the Evidence of Prevalence, Characteristics, and Prognosis in Primary Care? A Systematic Review of the Literature. *J Pain.* 2017;18(11):1295‐1312. doi:10.1016/j.jpain.2017.04.012

17 Konstantinou K, Beardmore R, Dunn KM, et al. Clinical course, characteristics and prognostic indicators in patients presenting with back and leg pain in primary care. The ATLAS study protocol. *BMC Musculoskelet Disord*. 2012;13:4. Published 2012 Jan 20. doi:10.1186/1471-2474-13-4

18. Konstantinou K, Dunn KM, Ogollah R, et al. Characteristics of patients with low back and leg pain seeking treatment in primary care: baseline results from the ATLAS cohort study. *BMC Musculoskelet Disord.* 2015;16:332. Published 2015 Nov 4. doi:10.1186/s12891-015-0787-8

19. Chou R, Qaseem A, Snow V, et al. Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society [published correction appears in Ann Intern Med. 2008 Feb 5;148(3):247-8]. *Ann Intern Med*. 2007;147(7):478‐491. doi:10.7326/0003-4819-147-7-200710020-00006

20. Mercer C, Finucane L. Examination of the lumbar region. In: Petty, N.J., (ed) Neuromusculoskeletal Examination and Assessment: A Handbook for *Therapists*. 4th edition (p317-335): Elsevier Health Sciences.

21. Koes BW, van Tulder MW, Peul WC. Diagnosis and treatment of sciatica. BMJ. 2007;334(7607):1313‐1317. doi:10.1136/bmj.39223.428495.BE

 22. Konstantinou K, Hider SL, Vogel S, et al. Development of an assessment schedule for patients with low back-associated leg pain in primary care: a Delphi consensus study. *Eur Spine J*. 2012;21(7):1241‐1249. doi:10.1007/s00586-011-2057-2

23. Stynes S, Konstantinou K, Dunn KM, et al. Reliability among clinicians diagnosing low back-related leg pain. *Eur Spine J*. 2016;25(9):2734‐2740. doi:10.1007/s00586-015-4359-2

24. Ware JE Jr. SF-36 health survey update. *Spine* (Phila Pa 1976). 2000;25(24):3130‐3139. doi:10.1097/00007632-200012150-00008

25. Dunn KM, Croft P, Jordan K. Recall of medication use, self-care activities and pain intensity: a comparison of daily diaries and self-report questionnaires among low back pain patients. *Prim Health Care Res Dev* 2010;11:93-102. [doi:10.1017/S1463423609990296](http://dx.doi.org/10.1017/S1463423609990296)

26. Roland M, Morris R. A study of the natural history of back pain. Part I: development of a reliable and sensitive measure of disability in low-back pain. *Spine* (Phila Pa 1976). 1983;8(2):141‐144. doi:10.1097/00007632-198303000-00004

27. Patrick DL, Deyo RA, Atlas SJ, et al. Assessing health-related quality of life in patients with sciatica. *Spine* (Phila Pa 1976). 1995;20(17):1899‐1909. doi:10.1097/00007632-199509000-00011

28. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983;67(6):361‐370. doi:10.1111/j.1600-0447.1983.tb09716.x

29. Nicholas MK. The pain self-efficacy questionnaire: Taking pain into account. *Eur J Pain*. 2007;11(2):153‐163. doi:10.1016/j.ejpain.2005.12.008

30. Ibrahim JG, Chu H, Chen MH. Missing data in clinical studies: issues and methods*. J Clin Oncol*. 2012;30(26):3297‐3303. doi:10.1200/JCO.2011.38.7589

31. StataCorp. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP, 2015.

32. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet*. 2007;370(9596):1453‐1457. doi:10.1016/S0140-6736(07)61602-X

33. Gierthmühlen J, Greinacher J, Höper J, et al. Sensory symptoms in low back pain - how do they matter? *Curr Med Res Opin.* 2017;24:1-12. [doi:10.1080/03007995.2017.1360851](http://dx.doi.org/10.1080/03007995.2017.1360851)

34. Walsh J, Hall T. Classification of low back-related leg pain: do subgroups differ in disability and psychosocial factors?. *J Man Manip Ther*. 2009;17(2):118‐123. doi:10.1179/106698109790824703

35. Schafer A, Hall T, Muller G, et al. Outcomes differ between subgroups of patients with low back and leg pain following neural manual therapy: a prospective cohort study. *Eur Spine J.* 2011;20:482-490. [doi:10.1007/s00586-010-1632-2](http://dx.doi.org/10.1007/s00586-010-1632-2)

36. Morsø L, Kent P, Albert H. Are self-reported pain characteristics, classified using the PainDETECT questionnaire, predictive of outcome in people with low back pain and associated leg pain? *Clin J Pain.* 2011;27:535-541. [doi:10.1097/AJP.0b013e318208c941](http://dx.doi.org/10.1097/AJP.0b013e318208c941%20%20)

37. Uher T, Bob P. Neuropathic pain, depressive symptoms, and C-reactive protein in sciatica patients. *Int J Neurosci.* 2013;123:204-208. [doi:10.3109/00207454.2012.746335](http://dx.doi.org/10.3109/00207454.2012.746335)

38. Tutoglu A, Boyaci A, Karababa IF, et al. Psychological defensive profile of sciatica patients with neuropathic pain and its relationship to quality of life. *Z Rheumatol.*  2015;74:646-651. [doi:10.1007/s00393-014-1527-4](http://dx.doi.org/10.1007/s00393-014-1527-4)

39. Artus M, van der Windt D, Jordan KP, et al. The clinical course of low back pain: a meta-analysis comparing outcomes in randomised clinical trials (RCTs) and observational studies. *BMC Musculoskelet Disord.* 2014;15:68. [doi:10.1186/1471-2474-15-68](http://dx.doi.org/10.1186/1471-2474-15-68)

40. Green DJ, Lewis M, Mansell G, et al. Clinical course and prognostic factors across different musculoskeletal pain sites: A secondary analysis of individual patient data from randomised clinical trials. *Eur J Pain.* 2018; 22: 1057-1070. [doi:10.1002/ejp.1190](https://doi.org/10.1002/ejp.1190)

41. Hüllemann P, Keller T, Kabelitz M, et al. Pain Drawings Improve Subgrouping of Low Back Pain Patients. *Pain Pract.* 2017;17:293-304. [doi:10.1111/papr.12470](http://dx.doi.org/10.1111/papr.12470)

42. Worster A, Carpenter C. Incorporation bias in studies of diagnostic tests: how to avoid being biased about bias. CJEM. 2008;10(2):174‐175. doi:10.1017/s1481803500009891

## Table, Figure legends

Table 1. Methods used to identify cases of neuropathic pain

Table 2. Baseline characteristics of patients with neuropathic pain based on s-LANSS

Table 3. Baseline characteristics of patients with neuropathic pain defined by clinical diagnosis of sciatica

Table 4. Baseline characteristics of patients with neuropathic pain based on a clinical diagnosis of sciatica and evidence of nerve root compression on MRI

Figure 1. Study flow diagram (adapted from Konstantinou et al 201518)

Figure 2. Venn diagram depicting the overlap between patients with and without neuropathic pain at baseline based on three case definitions

Figure 3. Clinical course of patients with and without neuropathic pain

1. Patients with neuropathic pain based on s-LANSS
2. Patients with neuropathic pain defined by clinical diagnosis of sciatica
3. Patients with neuropathic pain defined by clinical diagnosis of sciatica and evidence of nerve root compression on MRI

## List of Supplemental Digital Content

SDC\_Table 1.docx

SDC\_Table 2.docx

Table 1.

|  |  |  |
| --- | --- | --- |
| **Approach** | **Description of definition** | **Level of certainty** |
| **Clinical examination** | Clinical diagnosis of sciaticaa *with* evidence of possible or clear nerve root compression on MRI scan | Probableb |
| **Clinical examination** | Clinical diagnosis of sciatica a *without* evidence of nerve root compression on MRI scan | Possibleb |
| **Neuropathic pain screening tool** | S-LANSS score of ³ 12 | Possiblec |
| **Clinical examination** | Clinical diagnosis of referred leg pain | Unlikelyb |
| Abbreviations: MRI, magnetic resonance imaging; s-LANSS, self-report version of Leeds Assessment for Neurological Symptoms and Signsa Described by Koes et al.21 Criteria for clinical diagnosis agreed by consensus by Konstantinou et al22b Described by Treede et al1and later updated by Finnerup et al14c Described by Smith et al5 |

Table 2.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Characteristics**a |  | **Neuropathic pain** **(s-LANSS ³ 12)** |  | **Unadjusted odds ratio****(95% CI)** |
|  |  | *Yes,* *n=293* *(48.4%)* | *No,* *n=313 (51.7%)* |  |
| **Sociodemographic characteristics** |  |  |  |  |
| Female (n=606) |  | 200 (68.3) | 182 (58.2) | 1.55 (1.10, 2.16) |
| Age, mean (SD) (n=606) |  | 49.8 (13.5) | 50.4 (14.2) | 1.00 (0.99, 1.01) |
| Socio-economic status (n=590) | Higher managerial, administrative and professional occupations | 49 (17.4) | 79 (25.7) | 1 |
|  | Intermediate occupations | 71 (25.2) | 86 (27.9) | 1.33 (0.83, 2.14) |
|  | Routine and manual occupations | 142 (50.4) | 140 (45.5) | 1.64 (1.07, 2.5) |
|  | Never worked and long-term unemployed | 20 (7.1) | 3 (1.0) | 10.75 (3.03, 38.07) |
| Smoking status (n=605) | Never | 99 (33.9) | 127 (40.6) | 1 |
|  | Ex-smoker | 80 (27.4) | 105 (33.6) | 0.98 (0.66, 1.45) |
|  | Current | 113 (38.7) | 81 (25.9) | 1.79 (1.21, 2.64) |
| BMI (kg/m2),mean (SD) (n=598) |  | 29.7 (6.1) | 29.5 (5.6) | 1.01 (0.98, 1.03) |
| **Health status** |  |  |  |  |
| Self-reported diabetes (n=606) |  | 25 (8.5) | 22 (7.0) | 1.23 (0.68, 2.24) |
| Self-reported general health (n=605) | Excellent/ very good | 52 (17.8) | 93 (29.7) | 1 |
|  | Good | 93 (31.9) | 78 (24.9) | 2.13 (1.35, 3.36) |
|  | Fair | 116 (39.7) | 123 (39.3) | 1.69 (1.10, 2.58) |
|  | Poor | 31 (10.6) | 19 (6.1) | 2.92 (1.50, 5.67) |
| Fatigue (n=593) |  | 214 (74.3) | 198 (64.9) | 1.56 (1.10, 2.23) |
| Sleep difficulties (n=601) |  | 258 (88.4) | 253 (81.9) | 1.68 (1.06, 2.66) |
| **Pain characteristics** |  |  |  |  |
| Back pain intensity (0-10), mean (SD) (n=600) |  | 5.5 (1.6) | 5.1 (1.6) | 1.15 (1.04, 1.27) |
| Leg pain intensity (0-10) mean (SD), (n=578) |  | 5.8 (2.3) | 4.7 (2.4) | 1.20 (1.12, 1.29) |
| Constant pain symptoms (n=594) |  | 221 (75.4) | 177 (58.8) | 2.15 (1.51, 3.06) |
| Pain described as burning pain (n=606) |  | 165 (56.3) | 55 (17.6) | 6.05 (4.18, 8.77) |
| Duration of back pain symptoms in current episode (n=604) | < 6 weeks | 98 (33.7) | 119 (38.0) | 1 |
|  | 6 to 12 weeks | 65 (22.3) | 60 (19.2) | 1.32 (0.87, 2.04) |
|  | > 3 months | 128 (44.0) | 134 (42.8) | 1.16 (0.81, 1.66) |
| Duration of leg pain symptoms in current episode (n=580) | < 6 weeks | 110 (39.3) | 141 (47.0) | 1 |
|  | 6 to 12 weeks | 61 (21.8) | 58 (19.3) | 1.18 (0.75, 1.86) |
|  | > 3 months | 109 (38.9) | 101 (33.7) | 1.41 (0.96, 2.08) |
| Widespread pain b (n=590) |  | 124 (42.9) | 125 (41.5) | 1.05 (0.74, 1.47) |
| Leg pain worse (n=604) |  | 138 (47.4) | 139 (44.4) | 1.13 (0.82, 1.56) |
| Pain location (n=606) | Pain below the knee  | 228 (77.8) | 200 (63.9) | 1.98 (1.38, 2.87) |
|  | Pain in one leg | 211 (72.0) | 244 (78.0) | 0.73 (0.50, 1.06) |
| **Limitations in activities, participation and risk of persistent disabling pain** |  |  |  |  |
| LBLP-related disability (RMDQ, 0-23), mean (SD) (n=606) |  | 13.8 (5.6) | 11.5 (5.6) | 1.08 (1.05, 1.11) |
| Risk of persistent disability due to back pain (STarT Back) (n=530) | Low risk | 29 (10.2) | 53 (17.6) | 1 |
|  | Medium risk | 120 (42.3) | 154 (51.0) | 1.57 (0.92, 2.7) |
|  | High risk | 135 (47.5) | 95 (31.5) | 2.7 (1.56, 4.7) |
| **Psychological characteristics**  |  |  |  |  |
| Depression (HADS) (n=606) | Normal (0 to 7) | 155 (52.9) | 235 (75.1) | 1 |
|  | Possible (mild) cases (8 to 10) | 67 (22.9) | 52 (16.6) | 1.95 (1.29, 2.96) |
|  | Probable (moderate/severe) cases (≥11)  | 71 (24.2) | 26 (8.3) | 4.14 (2.53, 6.78) |
| Anxiety (HADS) (n=604) | Normal (0 to 7) | 118 (40.6) | 196 (62.6) | 1 |
|  | Possible (mild) cases (8 to 10) | 60 (20.6) | 60 (19.2) | 1.66 (1.08, 2.54) |
|  | Probable (moderate/ severe) cases (≥11) | 113 (38.8) | 57 (18.2) | 3.30 (2.22, 4.87) |
| Pain self-efficacy (PSEQ, 0-60) c (n=590), mean (SD) |  | 30.8 (14.6) | 37.4 (13.8) | 0.97 (0.96, 0.98) |
| **Neurological examination findings** |  |  |  |  |
| Muscle strength d (n=606) | 5/5 | 231 (78.8) | 270 (86.3) | 1 |
|  | 4/5 | 56 (19.1) | 36 (11.5) | 1.81 (1.15, 2.86) |
|  | 0 to 3/5 | 6 (2.1) | 7 (2.2) | 1.00 (0.33, 3.02) |
| Reflex (tendon) change (n=606) | None | 222 (75.8) | 265 (84.7) | 1 |
|  | Slightly reduced | 19 (6.5) | 11 (3.5) | 2.06 (0.96, 4.43) |
|  | Significantly reduced or absent | 52 (17.8) | 37 (11.8) | 1.68 (1.06, 2.65) |
| Sensation to pin-prick in the leg(s) (n=606) | Normal | 150 (51.2) | 204 (65.2) | 1 |
|  | Reduction or loss to pin-prick | 143 (48.8) | 109 (34.8) | 1.78 (1.29, 2.47) |
| Presence of allodynia or hyperalgesia in the leg(s) e (n=606) |  | 40 (13.7) | 17 (5.4) | 2.75 (1.52, 4.97) |
| Neural tension test f (any positive test, n=606) |  | 168 (57.3) | 165 (52.7) | 1.21 (0.87, 1.66) |
| Pins and needles in the leg(s) (n=606) |  | 209 (71.3) | 84 (28.7) | 5.80 (4.08, 8.23) |
| Pain affects the colour of patients skin (n=606) |  | 61 (20.8) | 6 (1.9) | 13.45 (5.70, 31.7) |
| **Neuroimaging** |  |  |  |  |
| Clear or possible nerve root compression (n=551) |  | 142 (52.8) | 154 (54.6) | 0.93 (0.66, 1.30) |
| **Pain medications**  |  |  |  |  |
| Number of pain medications g (n=606) | None | 34 (11.6) | 49 (15.7) | 1 |
|  | One | 103 (35.2) | 141 (45.1) | 1.05 (0.63, 1.75) |
|  | Two or more | 156 (53.2) | 123 (39.3) | 1.83 (1.11, 3.01) |