Low back pain - primary care approach

A prognostic approach to defining chronic pain: Replication in a UK primary care low back pain population

Pseudoradicular and radicular low-back pain - A disease continuum rather than different entities? Answers from quantitative sensory testing

A systematic literature review of psychological factors and the development of late whiplash syndrome

Dysmenorrhea: Contemporary perspectives
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This year has been dedicated as the “Global year against pain in women”. A series of documents has been composed by expert members of the IASP dealing with different aspects of pain experienced by women. It has become apparent that over 75% of first-time visits to a practitioner are because of pain. The practitioner is often not aware that he or she is treating pain as it is considered that the condition is simply a headache, abdominal ache, or indeed a pelvic problem. Without realising it the practitioners are treating pain. I have included the document on dysmenorrhoea as this is probably one of the most common complaints seen by general practitioners and gynaecologists. In future editions of the Journal I shall include many more of these topics regarding pain in woman.

Another commonly seen problem is that of backache. While most of us will immediately consider this to mean lower backache we must remember neck pain also constitutes back pain. Practitioners are often confronted by patients complaining of neck pain following motor vehicle accidents. The diagnosis of a whiplash injury is fairly simple but what of the late onset pain following the incident, the so-called late whiplash syndrome. In many cases this is simply attributed to psychological factors. The article by Williamson examines this condition and reaches rather surprising conclusions.

More frequently we are faced by patients with lower back pain. We are all aware then there are a multitude of causes for this condition. Freyhagen attempts to distinguish between radicular and pseudoradicular pain and questions whether these are not one and the same thing. Dunn attempts to use a prognostic approach to define chronic pain and who will suffer from this problem. From both these authors we can see the diagnosis still remains a problem because of the lack of a gold standard. They demonstrate that there is a poor correlation between the radiological findings and the clinical symptoms. We also note that other neurophysiological tests lack specificity. This big is the question whether we should use a triad of clinical tests: active flexion in the standing position with passive cervical flexion, a straight-leg raise test with dorsiflexion of the foot, and a straight-leg raise test with passive cervical flexion.

Meyer has written a useful guide to the primary care physician who is faced with the problem of the patient presenting with lower back pain. He does not try to deal with all the controversies but rather gives a practical approach which is clinically invaluable to the primary care physician.

Please remember to diarise the dates for our 3rd PAINSA Congress to be held at the Sandton Convention Centre from 29 August to 31 August 2008.

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Target co-morbid conditions in Neuropathic Pain*1

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Functional impairment

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INTRODUCTION

John F Bonica recognized that the complexity of pain management was mostly beyond the knowledge and skills of a particular healthcare provider.¹ In treating thousands of patients with chronic pain after World War 2, he emphasized that appropriate pain management should be based on the contribution of research scientists and various clinicians. He established the first interdisciplinary pain clinic in 1947 at the University of Washington in Seattle in the United States of America.

The gate-control theory of pain mechanisms published by Melzack and Wall in 1965, had a profound influence in the field of pain research and in the development of various forms of pain therapy.² This theory integrated the views of neurophysiology and psychology and states that spinal transmission of pain impulses is continuously modulated by various mechanisms including descending messages from the brain that originate in the cerebral cortex and brainstem. The descending pain inhibitory pathway involves the action of endogenous opioids and neurotransmitters, including serotonin and noradrenalin – this system is responsible for such diverse events as the action of opioids and certain anti-depressants, and the benefits of cognitive-behavioural therapy.³ The descending pathways are influenced by limbic system input, and a relaxed person is likely to experience less pain than an anxious/depressed individual.

The biomedical approach regards a specific pathway as the source of pain and pain is seen as a warning signal of tissue injury, likely to be aggravated by physical activity. If conservative treatment fails, some surgical technique will then be able to “correct” the problem.⁴,⁵

The modern paradigm of pain management has moved from this biomedical to the broader biopsychosocial approach, where pain mechanisms now integrate input from sensory, emotional and cognitive systems.

In the biopsychosocial model of chronic pain, bio- refers to the sensory or physical component of pain, psycho- refers to psychological factors (e.g. anxiety and depression) that impact on pain perception; and social- recognizes the importance of interpersonal relationships, work environment etc, on the pain process.⁶ Emotional factors may have a profound effect on pain perception and depression may lower the tolerance threshold for pain perception. Pain is therefore not a reflex, but a perceptual experience with emotional and motivational components.

Biopsychosocial model of pain⁴,⁶

Acute Pain is a normal biological response to injury / tissue trauma and a signal of ongoing or impending tissue damage and contributes to survival by protecting the organism from further injury.

Chronic Pain has been defined as “pain that persists for longer than the time expected for healing, usually taken to be three months.”⁶

Chronic pain often persists long after the tissue trauma that triggered its onset, has resolved and may be present in the absence of identified ongoing tissue damage or a previous history. Chronic pain is often a dysfunctional response which does not warn the individual of underlying disease or injury. However, it may cause severe suffering and reduced quality of life and has often been labelled a “disease in its own right”.⁹,¹⁰,¹¹

Primary Types of Pain⁹,¹¹

• Nociceptive pain (e.g. trauma, osteo-arthritis)
  Nociceptive pain occurs when intact peripheral nerve endings (nociceptors) are stimulated by noxious stimuli which include mechanical and inflammatory impulses.

• Neuropathic pain
  Neuropathic pain is due to a lesion in the peripheral or central nervous system, e.g. in nerve damage after trauma / surgery, spinal cord injury, etc.

• Dysfunctional pain
  There is a large group of chronic pain patients where no peripheral abnormality or neurological deficit can be detected. The mechanism of pain is abnormal sensory
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processing of non-painful stimuli and include idiopathic pain disorders such as post-whiplash disorders and fibromyalgia syndrome. There is growing evidence that the onset of these disorders may be associated with both physical and emotional triggers which may initiate pain in individuals with a genetic susceptibility.12

Both neuropathic and dysfunctional pain may be present in the absence of any obvious peripheral stimulus or “organic cause”.

• Mixed pain

Common mixed pain disorders include patients with cancer pain and low back pain (in particular low back pain following surgery, or failed back surgery syndrome) where neuropathic, nociceptive and myofascial components may contribute to the patient’s pain experience.

Not all patients with chronic pain have similar mechanisms, therefore a specific analgesic will not be equally effective for all different pain disorders.

LOW BACK PAIN

Low back pain (LBP) is among the most common reasons for visits to a physician with an explosion in prevalence in industrialized countries over the past few decades. The economic costs of this epidemic are astounding, some estimates that it annually exceeds 50 billion dollars in the United States alone.14,15

Low back pain (LBP) refers to spinal and paraspinal symptoms in the lumbosacral area and may be classified as follows:14,15

Acute LBP: Duration of less than 2-4 weeks
Subacute LBP: Up to 12 weeks
Chronic LBP: More than 12 weeks

ACUTE LOW BACK PAIN

Acute LBP has a favourable natural history. It is mostly a self-limiting disease and in 70% of patients will clear up in 2-3 weeks, 95% will resolve with conservative treatment within 6-8 weeks. However recurrences and persistence of low grade symptoms are also common, and occur in 25-50% of patients.16,17 With this high prevalence, appropriate care in the primary care setting is essential.

The etiology of acute LBP mostly remains uncertain and a diagnostic triage has been recommended for the initial evaluation as follows:17

1. Simple backache: this is the common non-specific LBP which is “mechanical” (varies with posture or movements) and of musculo-skeletal origin. Causes include facet joint syndrome and myofascial pain syndrome.14

2. Nerve root pain: well localized pain down one leg in a dermatomal pattern, radiating below the knee and often into the foot and toes, associated with other features of the lumbar root syndrome. A common mistake is to assume that all leg pain is of nerve root origin (“sciatica”) due to disc prolapse. Most leg pain has nothing to do with disc prolapse and is referred pain from muscles, ligaments, facet joints and myofascial trigger points.17,18

More than 90% of lumbar disc herniations occur at the L4/L5 and L5/S1 levels. A focused clinical examination should include straight-leg-raise testing, evaluation of knee strength and reflexes (L4 root), great toe and foot dorsi-flexion strength (L5 root), foot-plantar-flexion and ankle reflexes (S1 root) and the distribution of sensory symptoms.

3. Possible serious spinal pathology: Red flag conditions such as tumours and infections are extremely rare, accounting for less than 1% of presentations in primary care.15,17 It is however, important to exclude these and to assure the patient that there is nothing seriously wrong. These serious causes of LBP can be recognized from the history and clinical examination and do not require screening investigations.14,15,18,19,20

Guided by the history, the clinical examination includes:

• General observation of the patient
• Abdominal / pelvic / vascular screening
• Regional back examination
• Neurological screening, including testing for sciatic nerve irritation

Red flags in LBP (indicative of major spinal pathology)17,21

• Pain is constant, progressive, “non-mechanical” (doesn’t improve with position / rest)
• Presentation age: <20 years or >55 years
• Previous history
  Carcinoma, HIV
  Systemic steroids
  Drug abuse
  Violent trauma

• Weight loss
• Thoracic pain
• Structural deformity
• Cauda equina syndrome

Cauda equina syndrome (CES) is a rare but serious condition and a surgical emergency. CES is a collection of signs and symptoms resulting from compression of the bundle of nerve roots emerging from the end of the spinal cord below the first lumbar vertebra, e.g. due to a massive central disc prolapse on this level. The classic syndrome is characterized by severe LBP and bilateral “sciatica”, associated with “saddle” anesthesia around the anus and perineum and bladder and bowel dysfunction e.g. urinary retention or overflow urinary incontinence in the presence of marked bladder distention.22 Patients with acute LBP and / or radicular pain must be warned that loss of visceral function may occur and that urgent medical attention and management is then essential.22

The focus of medical attention in patients with LBP has for decades been on the nerve / disc / vertebra complex, with little or no attention given to the soft tissue component. The soft tissue component may be a major culprit in producing LBP and a soft tissue examination may identify musculo-
skeletal and myofascial syndromes. Myofascial pain syndrome is often underdiagnosed and misunderstood in clinical practice and may closely mimic radicular syndromes, e.g. gluteus minimus pain may radiate down the posterior or latera part of the leg and may reach the ankle, interfering with walking and simulating a L₁-L₃ or L₅-S₁ radiculopathy.

After the diagnostic triage has been performed, the following 2 questions should be answered:

- **Is the LBP originating in the spine?**
  - Low back pain may be part of a systemic musculo-skeletal / rheumatological disorder, e.g. ankylosing spondylitis or rheumatoid arthritis and "markers" include:
    - Gradual onset of LBP before 40 years of age
    - Peripheral joint involvement
    - Marked morning stiffness
  - Family history
  - LBP may be caused by abdominal or pelvic organs, but these patients will mostly have gastrointestinal, urinarian, vascular or gynaecological symptoms:
    - Pelvic organs: prostatitis, endometriosis
    - Renal disease: pyelonephritis, renal calculus
    - Vascular disease: aortic aneurysm
    - Gastro-intestinal: pancreatitis

Back pain is mostly the prominent symptom with a true low back problem and the patient will mostly have other low back symptoms/signs, e.g. stiffness and tenderness.

- **Are there psychosocial barriers to recovery?** ("Yellow flags")

Early identification and management of yellow flags may be helpful in limiting the chronicity of LBP and also reduce the potential to develop disability. Psychosocial factors may have more impact than biomedical or biomechanical factors as risk factors for LBP, and include:
  - Belief that LBP is harmful/disabling
  - Fear-avoidance behaviour / reduced activity
  - Depressed mood / social withdrawal
  - Reliance on passive treatment vs. active participation

**NB:** *Facial expressions* of health care providers and "threatening" diagnostic labels (e.g. "degenerative changes", "disc protrusion", etc.) may activate the fear network and intensify the pain experience.

Blue flags are occupational factors that may influence the presentation of LBP and include:
  - Physically and psychologically demanding jobs
  - Job dissatisfaction
  - Medico-legal and disability issues
  - Poor employer – employee relations
  - The misconception that you have to be pain-free to return to work.

**Investigating a patient with acute low back pain**

The diagnostic triage approach outlined above is based on clinical assessment and imaging is mostly not warranted, unless specifically indicated by the presence of red flags. It has been known for years that there is a poor correlation between LBP and X-ray findings, yet patients are often given a diagnosis of "degenerative arthritis" which they have to "carry" for the rest of their lives and which may even reinforce illness-behaviour.

The Royal College of Radiologists recommend that x-rays should be reserved for:
  - Non-resolving symptoms (+ 4-6 weeks)
  - Deteriorating symptoms
  - Neurological signs
  - History of trauma

The yield from plain radiographs are low, even with these indications and may anyway miss early tumours, spinal infections, herniated disc and most cases of nerve root irritation.

In the absence of red flags, imaging studies and further testing are mostly not helpful during the first 4 weeks of acute LBP.

Advanced radiographic studies such as computerized tomography (CT) or magnetic resonance imaging (MRI) should be obtained when the clinical evaluation suggests a serious cause of LBP. For patients with sciatica, early imaging is unnecessary unless neurological abnormalities are identified. It is well known that findings such as bulging and herniated discs and spinal stenosis are observed in up to 50% of normal and asymptomatic individuals.

Prompt work-up with CT or MRI is recommended in patients with severe or progressive neurological deficit or when a serious underlying condition is suspected (e.g. vertebral infection or cauda equine syndrome).

Radio-isotope studies can be used to evaluate for infection or fractures not noted on plain radiographs.

Other laboratory studies such as the erythrocyte sedimentation rate (ESR), complete blood count, urinalysis and markers for inflammatory disorders (e.g. HLA-B27 for ankylosing spondylitis) are of value in specific patients to exclude other causes of LBP.

The assessment and diagnostic triage of a patient with acute LBP is based on clinical evaluation and even the best image can't substitute an appropriate clinical assessment.

**Management of a patient with simple acute low back pain:**

General principles:
  - Since the early 1990’s, the era of routine radiography, strict bed rest and traction has been replaced by selective imaging, and an early return to normal activities to prevent recurrences and chronic LBP.
• Early activity, even in the presence of some pain, is recommended rather than the traditional principle of “let pain be your guide”.13,33

• The modern epidemic of work disability due to chronic LBP in most developed countries is a serious problem, and some authorities fear that inappropriate medical management of acute LBP has contributed to this phenomenon.11

• Management according to evidence-based guidelines includes early implementation of the biopsychosocial approach and focuses on explanation, addressing patients’ concerns and fears and encouraging and supporting patients to resume normal activities.15

• Patients should be informed of the generally favourable prognosis of acute LBP with or without sciatica. In the absence of red flags, there is mostly no need for special investigations, studies since 90% of patients will recover spontaneously within 4 weeks.12 Clinicians should explain that routine imaging and other tests usually cannot identify a definite cause and do not improve patient outcomes.20

• The overall goals in the management of the patient with acute LBP is symptomatic control of pain and the prevention of chronic LBP and/or disability.11

• A fundamental aspect of this approach is to return to normal activity and work (with modification of some activities) even with some degree of pain. Both the primary care doctor and physiotherapist play a crucial role in this approach, and may need the assistance of an occupational therapist.11

**Medication:**

Nonsteroidal anti-inflammatory drugs (NSAIDs and COXIBs) and paracetamol are the drugs of choice. Paracetamol is a slightly weaker analgesic than NSAIDs / COXIBS but a reasonable first-line option from the treatment of acute LBP because of a favourable safety profile and low cost.26 Muscle relaxants are mostly not more-effective and short-term use of Tramadol or an appropriate opioid may be considered in patients with severe pain not controlled with paracetamol or NSAIDs / COXIBS.14,30

**Resume normal activities:**

Activity modification is now the preferred recommendation with 2 or 3 days of bedrest reserved for patients with acute sciatica. For patients with simple backache, continuation of usual activity is recommended, avoiding specific activities that provoke pain.14,30

**Role of physiotherapist:**

• Patient education e.g. self-care and posture

• Identifying red/yellow/blue flags and appropriate management and referral

• Incorporate the principles of cognitive behavioural therapy, which include

  - Promote positive attitudes to work and exercise
  - Be aware of depression / distress

  DO NOT CATASTROPHIZE

Activity alteration / appropriate exercise programme in accordance with biokineticist and occupational therapist. Low impact aerobic activities, e.g. walking and cycling are the best early activities. More strenuous activity such as climbing and jogging should be avoided in the acute phase. Specific back and strengthening exercises may worsen symptoms in the acute phase, and may be gradually phased in after the first 2 weeks to prevent chronic pain and disability.14,37

• Spinal manipulation has small to moderate short-term benefits in the first month of acute LBP without radiculopathy.17

• Other modalities such as ultrasound, traction, laser treatment and transcutaneous electrical nerve stimulation (TENS) have no proven efficacy in acute LBP.

The physiotherapist plays a crucial role in education which empowers patients to take control over their back pain, minimize catastrophizing and to restore confidence in the patient’s ability to recover.

**Referral for surgery in the first 3 months:**14,37

• Cauda equina syndrome is a surgical emergency.

• The natural history of lumbar disc herniation with radiculopathy is often for improvement over a period of 4 weeks.

  - Nerve root compression / sciatica may be considered for surgery if there is (progressive) neurological deficit or all 4 of the following criteria are met:

    - Leg pain is worse than back pain
    - Positive straight-leg-raise test
    - No response to conservative therapy:
      - 4-6 weeks for herniated disk
      - 8-12 weeks for spinal stenosis
  - Imaging shows lesion that correlates with symptoms

**Interdisciplinary Approach**

Persistence of acute pain beyond 6 weeks is an indication for more concerted intervention and most guidelines will recommend an interdisciplinary approach. The key issue is that the intervention must be closely related to the workplace with the specific goal of returning to work. Worksite intervention functional restoration has been shown to be the critical component of interdisciplinary intervention for subacute LBP.14,34,35

**CHRONIC LOW BACK PAIN**

Chronic low back pain is a common disorder and may be present in up to 39% of adults.36 Although extensive searching for a specific organic diagnosis such as herniated disc, annular tears, spondylolisthesis, facet joint osteoarthritis, etc. is often performed, these commonly identified changes seen in radiographs, CT and MRI scans,
only have weak correlations with the presence of chronic LBP and patients may undergo inappropriate surgery for this reason.37 The risk factors for chronicity in chronic LBP include psychosocial factors such as psychological distress and depression, abnormal illness behaviour, medico-legal proceedings, low job satisfaction, prolonged period off work and personal problems – therefore the majority of patients with chronic LBP need a biopsychosocial interdisciplinary approach to their management.35,36

Treatment goals for patients with chronic LBP include:17
• Reduce pain intensity
• Maintain physical activity
• Maximize functional abilities in the presence of persistent pain
• Return to work
• Reduce misuse of inappropriate medications
• Increase the patient’s ability to self-manage his/her pain

Interdisciplinary management15,17,24,40
A definite organic cause of chronic LBP cannot be determined in the majority of patients – therefore a comprehensive biopsychosocial and interdisciplinary approach is mostly followed, focussing on functional improvements.

The last two decades has seen a radical shift in the understanding and management of chronic LBP, from the biomedical model of specific organic pathology / structural damage and physical “fixes”, to the comprehensive biopsychosocial model, with emphasis on restoration of function. The rehabilitative approach has emerged and emphasizes restoration of normal function. This approach also addresses abnormal pain-behaviour, where patients may become convinced that their pain is disabling are refractory to being cured, consequently they adopt the social role of a “victim”.

Education
The primary care doctor plays a critical role in this regard. The healthcare professional and patient must have realistic expectations regarding making a specific diagnosis and providing effective analgesia. Chronic LBP has a high recurrence rate, but is not associated with progressive tissue damage. Relief of pain without increased activity will not solve the problem.

Exercise / Physical therapy / Occupational therapy
Several studies support the effectiveness of exercise in the treatment of non-specific chronic LBP, but there is currently no consensus on the most effective programme design to maintain exercise benefits. Long-term maintenance of benefits also require patient education and motivation towards behavioural change and long-term compliance – programme supervision improves compliance.46

Exercise programmes include aerobic conditioning, postural training, stretching, strengthening and a home exercise programme for the individual, which is vital. The value of strengthening exercises has been highlighted by various authors, emphasizing the importance of strengthening of the lumbar spine extensors as well as abdominal strengthening.30-44 It has been shown that a carefully conducted specific strength training programme resulted in a significantly reduced need for spinal surgery in a population of symptomatic patients, mainly with lumbar disc problems.35

Supervised exercise therapy is strongly recommended as a first-line treatment in the management of chronic LBP. A graded exercise programme as part of a cognitive-behavioural approach seems the most appropriate approach. Exercise decreases fear-avoidance behaviour and may improve functioning in the presence of ongoing pain.21

Other moderately effective non-pharmacological therapies for chronic LBP include acupuncture message therapy and manipulation.24,41

Occupational therapy involves vocational adjustment disability management when indicated and then includes workplace analysis and work-specific reconditioning (“hardening”).

Cognitive behavioural therapy aims to address maladaptive behaviours, beliefs and negative thinking patterns. High levels of pain catastrophizing (e.g. magnification and helplessness) are associated with a more intense pain experience, more emotional distress and disability and should be addressed appropriately.32

Mood and somatoform disorders are important in a group of chronic LBP patients and should then be managed appropriately.

Medication
• Chronic LBP is mostly multi-factorial and may be nociceptive, neuropathic, myofascial, dysfunctional or a combination of these mechanisms (e.g. failed back surgery syndrome). It therefore remains difficult to adhere to a strict algorithm for all patients with chronic LBP.
• Nociceptive pain is usually treated with anti-inflammatory or analgesic medications.
• Neuropathic pain is treated with medications that influence neuro-transmitters, e.g. antidepressants and anticonvulsants.
• Current evidence supports the use of strong opioids in a carefully selected subset of chronic LBP patients. A detailed assessment and monitoring by an experienced pain clinician is necessary when strong opioids are prescribed and only sustained-release opioids e.g. transdermal fentanyl and substanied release oral morphine should be used.49

Invasive therapy47
• Nerve blocks may assist to improve pain control and enable patients to start active exercise.17,26 Epidural steroid injections give short-lived pain relief for a minority of patients with radicular symptoms. Facet joint injections with a corticosteroid may also provide
short-term pain relief when a facet joint is the source of back pain. There is limited evidence that injection of the sacro-iliac joint with cortico-steroids may relieve LBP from this origin for a short time.

- Numerous percutaneous and minimally invasive techniques to treat discogenic pain, lumbar facet syndrome, post-laminectomy syndrome etc. have been introduced over recent years. Most efficacy data is still based on limited case series reports and retrospective studies and prospective randomized controlled trials are necessary. Pulsed radiofrequency may be indicated for cervical more than lumbar pain in well selected patients – however, more evidence is necessary before official recommendation for this procedure in guidelines will be appropriate.

- Spinal surgery does have a place in the management of chronic LBP – however, patient selection must be very strict, and a second or even third conservative opinion is recommended before surgery is considered. Inappropriate patient selection is a major contributory factor to the catastrophic and common complication of failed back surgery syndrome. Patients with progressive neurological deficit and/or symptoms of cauda equina syndrome deserve early intervention.

CONCLUSION:

More than 85% of patients who present to primary care with chronic LBP, cannot be attributed to a specific cause or spinal abnormality (non specific or simple LBP). Consequently, the treatment of chronic LBP is mostly not primarily focused on removing or correcting an underlying organic pathology, but at the reduction of disability through modification of environmental factors, supervised exercise and cognitive adjustment.

In his 1987 Volvo award-winning paper, “A new clinical model for the treatment of low back pain”, Waddell stated that “controlled exercises not only restore function, reduce distress and illness behaviour, and promote return to work, but actually reduce pain”. Since this publication and his major comprehensive text which was often referred to in this review, scientific evidence and consensus opinion have continued to demonstrate the superiority of active care to the traditional passive care approach.

REFERENCES

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A prognostic approach to defining chronic pain: Replication in a UK primary care low back pain population

Kate M. Dunn a,*, Peter R. Croft a, Chris J. Main a, Michael Von Korff b

a Primary Care Musculoskeletal Research Centre, Keele University, Staffordshire ST5 5BG, UK
b Group Health Cooperative, Center for Health Studies, Seattle, USA

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Abstract

A novel prognostic approach to defining chronic pain was developed in a US primary care low back pain population, using a combination of information about pain history, current status and likely prognosis. We tested whether this method was generalisable to a UK population. A prospective cohort of 426 patients who consulted with back pain at one of five UK general practices, and who returned follow-up information 1-year later were included. A baseline risk score was calculated based on pain severity and prognostic measures (depression, diffuse pain, pain duration), and cut-points from the US study applied for the risk of future clinically significant back pain, as defined by Chronic Pain Grades 2–4. New cut-points were also derived for the UK population using identical methods. The cut-points for probable and possible chronic pain developed in the US population (80% and 50% probability of future clinically significant back pain, respectively) were appropriate for the UK population, but the cut-point for classifying people at low risk (20% probability) was not replicated in the UK sample. The newly derived cut-points in the UK sample were similar; they remained the same for probable chronic pain, were slightly increased for possible chronic pain, and slightly reduced for those at intermediate or low risk. This method for defining chronic pain prospectively, using risk thresholds for future clinically significant pain, appears to be generalisable to a UK back pain population, particularly for identifying probable chronic pain, and may be generalisable to other primary care low back pain populations.

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Keywords: Chronic disease; Pain; Classification; Prognosis; Risk; Cohort studies; Prospective studies

1. Introduction

The term ‘chronic pain’ has a spectrum of meanings and interpretations. Conventional divisions, e.g. between acute and chronic pain, have been criticised (Von Korff et al., 1993; Waddell, 1998; Dunn et al., 2006a), and approaches to the different definitions compared (Von Korff and Miglioretti, 2005). Conventional definitions of chronic pain often use length of time since pain onset, e.g. 6-months (International Association for the Study of Pain, 1986), with no consideration of pain severity or disability and have limited underlying empirical research. Work investigating back pain episode duration has shown that this is an important prognostic factor, but the use of episode duration alone to classify ‘chronic’ back pain was not advocated (Dunn and Croft, 2006a). Defining chronic pain using pain history or current pain also does not fit well with the ‘yellow flags’ system of assessing psychosocial risk factors that is widely recognised in back pain (Kendall et al., 1997; Waddell and Turk, 2001; Samanta et al., 2003). Many of the ‘yellow flags’, including distress and somatisation, have been consistently shown as useful indicators of back pain prognosis.

* Corresponding author. Tel.: +44 1782 584703; fax: +44 1782 583911.
E-mail address: k.m.dunn@cphc.keele.ac.uk (K.M. Dunn).
URL: http://www.keele.ac.uk/research/phc/pcmrc/ (K.M. Dunn).

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2.2. Setting and sample

Consecutive patients aged 30–59 years seeking care for low back pain with five general practices in North Staffordshire during the study period (mid-October 2001 to mid-October 2002) had been invited to take part in a study of the prognosis of back pain, and 935 patients were recruited and followed for a 1-year period. The upper age limit of 59 years was intended to focus the sample on a working-age population. More information on patient recruitment is presented elsewhere (Dunn and Croft, 2005). The practices cover a heterogeneous population both socio-economically and geographically. Consent to follow-up was given by 776 baseline participants, and 466 completed the 12-month questionnaire. The analysis presented here is based on 426 participants for whom complete information on the relevant baseline and follow-up variables was available (46% of the initial baseline responders). There were no differences in the prevalence and distribution of baseline measures of risk between people with and without follow-up information; for example, mean baseline anxiety and depression scores for the included participants were 8.6 and 7.2, respectively, compared with 8.5 and 7.0 for the baseline participants on whom complete follow-up data were not available.

2.3. Data collection

Questionnaires eliciting baseline data were mailed soon after the index consultation, and the follow-up questionnaire was mailed 1-year later. The elements included in the baseline assessment of risk, as in the American study, were a mixture of pain status variables (including severity of pain and its impact in daily life, pain duration and the presence of pain elsewhere than the back) and a non-pain variable (depression). Pain status at baseline was derived from the Chronic Pain Grade (Von Korff et al., 1992), with the addition of questions about pain duration and widespread pain. We used the identical Chronic Pain Grade in the UK study, but different instruments had been used to measure pain duration, widespread pain and depression. Pain duration was determined through recall of the last pain-free month; there is evidence for the validity and reliability of this question (Dunn and Croft, 2006a; Dunn et al., 2006b). Pain elsewhere was assessed through recall of pain during the previous 2 weeks in the shoulder, arm, neck or head. Depression was assessed using the depression dimension of the Hospital Anxiety and Depression Scale (HADS; Zigmond and Snaith, 1983); the scale gives scores for anxiety and depression from zero (lowest) to 21 (highest psychological distress). Both the US and UK studies had used the Chronic Pain Grade to measure outcome at 1-year follow-up.

2.4. Statistical methods

We calculated a risk score from the baseline measures as described above and as identified by Von Korff and Miglioretti (2005), following their scoring rules as closely as possible. These scoring rules assigned 0 scores to low values on the baseline measures of pain status and depression.

2.4.1. Pain severity variables

Average pain intensity: 0–3 = 0; 4–6 = 1; 7–10 = 2.
Worst pain intensity: 0–4 = 0; 5–7 = 1; 8–10 = 2.
Current pain intensity: 0–2 = 0; 3–4 = 1; 5–10 = 2.
Interference with usual activities: 0–2 = 0; 3–4 = 1; 5–10 = 2.
Interference with work/housework activities: 0–2 = 0; 3–4 = 1; 5–10 = 2.
Interference with family/social activities: 0–2 = 0; 3–4 = 1; 5–10 = 2.
Days of activity limitation in the prior 6 months: 0–6 = 1; 7–14 = 2; 15–30 = 3; 31+ = 4.

2.4.2. Other prognostic variables

Pain duration responses were scored as: less than 3 months = 0; 3–6 months = 1; 7–12 months = 2; 1–2 years = 3; 3 or more years = 4.
The number of other pains was scored as: 0 = 0; 1 = 1; 2 = 2; 3 = 3; 4 = 4.

In order to derive comparable depression scores, the categories used for the SCL-90-R in the original Von Korff and Miglioretti (2005) paper were applied by us to a US general population sample to provide information on the proportion of the population in each category. We then applied these proportions to HADS scores derived from a UK general population sample, and corresponding categories on the HADS scores were derived. This gives scoring for the HADS of 0–3 = 0; 4–7 = 1; 8–10 = 2; 11–12 = 3; 13–21 = 4.

As in the original publication, we used Chronic Pain Grades 2–4 at 1-year follow-up as the criterion for clinically significant back pain at outcome, as this identifies persons who report significant pain and/or pain dysfunction at long-term follow-up.

First, the baseline cut-points defined in the US population were applied to our UK study population, the proportions of the population falling into each risk score group observed, and the proportions of each risk score group with clinically significant back pain (Chronic Pain Grades 2–4) at outcome (1-year follow-up) calculated.

Second, we used the same methods as the original publication to define cut-points at baseline for probable and possible chronic back pain. A probability plot was produced to show the ability of these baseline risk categories to predict clinically significant back pain at 1-year follow-up. The threshold baseline risk scores for probable and possible chronic back pain were set at 80% and 50% probability of a poor 12-month outcome, respectively. The plot was smoothed using a 5-point rolling average. Low and intermediate risk was defined by less than a 20% probability of chronic back pain.

3. Results

Baseline characteristics of the study sample are presented in Table 1. Fifty-six percent of the sample was female, and the mean age was 47 years. Just under half of the population continued education beyond the age of 16. Sixty-six percent of the sample reported being in employment at baseline; 44% of these were in routine or semi-routine occupations and 28% in professional or managerial occupations.
The mean baseline risk score was 16.0 (SD 6.2). Table 2 presents the proportions of people in each risk score group at baseline, in both the US and UK populations, using the cut-points derived in the US study. There is a clear difference between the two populations. Using

| Table 1 | Baseline characteristics of UK study population (n = 426) |
|-----------------|------------------|------------------|
| Age Mean age (years) (range; SD) | 46.6 (30–59; 8.2) |
| Gender [no. (%)] | Male 187 (43.9) | Female 239 (56.1) |
| Education [no. (%)] | Up to age 16 years 212 (49.8) | Beyond age 16 years 214 (50.2) |
| Employment [no. (%)] | Employed 279 (65.5) | Managerial/professional occupation 76 (27.7) | Intermediate occupations 42 (15.3) | Self-employed 15 (5.5) | Lower supervisory/technical occupation 21 (7.7) | Semi-routine/routine occupations 120 (43.8) | Not employed 145 (34.0) |
| Pain duration [no. (%)] | Less than 3 months 80 (18.8) | 3–6 months 51 (12.0) | 7–12 months 49 (11.5) | 1–2 years 69 (16.2) | 3 or more years 177 (41.6) |
| Chronic Pain Grade [no. (%)] | 0 – Pain free 5 (1.2) | 1 – Low disability, low intensity 94 (22.1) | 2 – Low disability, high intensity 83 (19.5) | 3 – High disability, moderately limiting 119 (27.9) | 4 – High disability, severely limiting 125 (29.3) |
| Hospital Anxiety and Depression Scale Mean anxiety score (range; SD) | 8.6 (0–21; 4.8) | Mean depression score (range; SD) | 7.2 (0–19; 4.6) |
Chronic back pain. The risk score corresponding to a score of 22 or more were classified as having probable clinically significant back pain, persons with a baseline risk criterion of 80% probability of observed future clinical significance at follow-up were relatively similar to those reported in the US study at intermediate risk or in the UK sample (Fig. 1). Using this plot, and the observed clinically significant back pain at follow-up risk scores were plotted against the probability of 11% of the US study sample.

Chronic Pain Grades 2–4 at 1 year, compared to only 23% of our UK sample in the low risk group had possible or probable chronic back pain categories at follow-up, compared with 51% in the UK study sample. However, whereas 31% of the US population were defined as being in the probable chronic back pain category, compared with 22% of the UK sample. Whereas 31% of the US population were defined as low risk, only 11% of the current sample fell into this category.

The proportion of the UK sample in each Chronic Pain Grade at 1 year follow-up is shown in Table 3. Forty-nine percent \((n = 210)\) would be defined as having clinically significant back pain by the criterion of being in Chronic Pain Grades 2–4 at follow-up.

In order to define potential new cut-points, baseline risk scores were plotted against the probability of observed clinically significant back pain at follow-up for the US sample (Fig. 1). Using this plot, and the criterion of 80% probability of observed future clinically significant back pain, persons with a baseline risk score of 22 or more were classified as having probable chronic back pain. The risk score corresponding to a 50% probability of significant back pain at follow-up was 18, meaning that people with a baseline risk score of 18–21 have possible chronic back pain. The cut-point for being at low risk is shown on the plot as a risk score of 4, indicating that people with a baseline risk score 4 or lower have a less than 20% probability of having chronic back pain. This procedure indicates that, at baseline, 22% would be classified as having probable chronic back pain, an additional 21% would be classified as having possible chronic back pain, and 52% and 5% would be classified as having intermediate and low risk of chronic back pain, respectively.

In order to define potential new cut-points, baseline risk scores were plotted against the probability of observed clinically significant back pain at follow-up for the UK sample (Fig. 1). Using this plot, and the criterion of 80% probability of observed future clinically significant back pain, persons with a baseline risk score of 22 or more were classified as having probable chronic back pain. The risk score corresponding to a
for probable chronic back pain, but the risk score cut-points for the other categories were slightly altered, leading to more appropriate classification of those at low risk (as determined by a lower proportion with clinically significant back pain at 1-year follow-up).

The conventional approach to defining chronic pain is usually based on episode duration of 3 or 6 months. We have previously examined the effect of episode duration on low back pain prognosis, and although it is important, a cut-point of 3 months was not useful, and a division around 3 years duration was more apparent than 1 at 6 months (Dunn and Croft, 2006a). The prognostic approach to defining chronic pain builds on this work by adding further information to the model. If we compare the two approaches directly, 52% and 56% of people with more than 3 or 6 months of pain, respectively, at baseline had clinically significant back pain at 1 year, compared to 67% of people with possible or probable chronic pain (51% and 90%, respectively). Although duration is clearly a major component of the prognostic approach, adding additional data improves the model, and the prognostic approach has higher sensitivity to identify people at risk of a poor outcome than a more traditional approach based purely on duration.

The prognostic approach to defining chronic pain raises issues regarding the labelling of patients. At present, patients are given labels according to how long they have had the condition, so a label of chronic pain may be given to people with more than 3 or 6 months of pain. This is a purely retrospective definition, gives the patient no indication of their likely prognosis, and leads to uncertainty. Our definition includes a measure of duration, but also combines this with other information about a patient’s current status, and provides an estimate of likely future status. Research suggests that patients with chronic pain conditions find the uncertainty of the current definitions of chronic pain very difficult in terms of their expectations and plans for the future, as well as their emotional acceptance of the condition (Richardson et al., 2006). This implies that defining chronic pain prospectively, and giving patients an estimate of their likely future status, may reduce uncertainty and potentially alleviate distress.

One limitation highlighted in the original US paper was the fact that it was based on a study sample drawn from a particular culture and healthcare system; we have now tested the study findings in another country and a different healthcare system, and found them to be broadly generalisable. Another potential limitation highlighted was that the original sample was a well-educated population. Our findings demonstrate that this is unlikely to limit the generalisability of the results, as less than half of our UK study population reported having continued education beyond 16 years, and yet the study

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**Table 5**

Distribution and characteristics of risk groups at baseline and probability of clinically significant back pain at 1-year by risk level determined at baseline by new cut-points

<table>
<thead>
<tr>
<th>Baseline risk score group</th>
<th>Proportion of population in group (%)</th>
<th>Baseline average pain intensity (mean, range)</th>
<th>Baseline HADS depression score (mean, range)</th>
<th>Percent (95% C.I.) with Chronic Pain Grade 2-4 back pain at 1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk (0–4)</td>
<td>4.5</td>
<td>2.5 (0–6)</td>
<td>1.6 (0–7)</td>
<td>10.5% (1.3, 33.1)</td>
</tr>
<tr>
<td>Intermediate risk (5–17)</td>
<td>52.3</td>
<td>5.1 (0–10)</td>
<td>5.2 (0–19)</td>
<td>32.7% (26.6, 38.9)</td>
</tr>
<tr>
<td>Possible chronic pain (18–21)</td>
<td>21.4</td>
<td>6.9 (3–10)</td>
<td>8.6 (1–18)</td>
<td>56.0% (45.2, 66.4)</td>
</tr>
<tr>
<td>Probable chronic pain (22+)</td>
<td>21.8</td>
<td>7.6 (3–10)</td>
<td>11.7 (2–19)</td>
<td>90.3% (82.4, 95.5)</td>
</tr>
</tbody>
</table>

---

**Fig. 1.** Probability of clinically significant back pain (Chronic Pain Grades 2-4) at 1-year predicted from baseline risk score.
findings were comparable. Further evidence for the wider generalisability of this method for defining chronic pain is given by the use in the two studies of different instruments measuring the prognostic indicators, episode duration and depression in particular. Despite different measures, the probabilities of chronic back pain were similar, the cut-point on a risk score for probable chronic back pain was identical in both populations and the cut-point for possible chronic back pain also only differed by two points on a 29-point scale. Although there was loss-to-follow-up in this study, our results are unlikely to be influenced by non-response bias. We applied the risk categories from the study populations to the whole baseline population, and the proportions of people in each category were identical to those in the sample used for this analysis (probable 21.0% vs. 21.8%; possible 21.3% vs. 21.4%; intermediate 52.5% vs. 52.3%; low 5.2% vs. 4.5%). In addition, brief data were collected on 90 non-responders to the 12-month questionnaire, and the outcomes of this group were identical to the sample with complete data, for example 27% of the complete responders said that they were much better or had completely recovered, compared with 26% of the brief responders.

One point that has arisen from this direct comparison of primary care low back pain consulters is the difference between samples drawn from US and UK consulting populations. Using the original risk score groups, 6% of the US primary care population were defined as having probable chronic back pain, whereas in this UK population, 22% were classified in the same group, nearly four times the amount. Similarly, whereas 31% of the US population were defined as low risk, only 11% of the current sample fell into this category. This difference is unlikely to be due to the methods used for identifying study participants, as sampling techniques (consecutive consulters) were comparable. It could potentially reflect differences in the risk of clinically significant back pain among primary care low back pain consulters in the two healthcare settings, or the difference may be a result of differing consultation patterns in the two healthcare systems. This supposition is supported by the fact that the UK sample had somewhat worse outcomes at 1 year than the US sample, with 49% of the UK sample having Grade II–IV back pain at 1 year, compared to 34% of the US sample (Von Korff et al., 1993). A second reason for observed differences may be that information was collected from UK study participants at a time closer to the consultation, as many risk factors for poor prognosis are known to fall following consultation (Dunn and Croft, 2006b). Data in the original study were collected 3–6 weeks post consultation, whereas data in the current study were obtained 1–3 weeks after the consultation (Dunn and Croft, 2005). Evaluation of the validity of a prognostic approach to defining chronic back pain at the time of the initial visit is an issue for future research, as it is likely that higher proportions of patients would fall in the probable and possible chronic pain categories. This suggests a caveat about the assessment of chronic pain status. A prognostic approach to classification of chronic pain may be most useful at a follow-up visit occurring several weeks to a month after an initial back pain visit. At the time of an initial visit, it is reasonable to expect substantial improvement in pain status in the next week or two, although the large majority of patients will not become pain-free (Von Korff et al., 1993). The proposed approach to prognostic assessment of risks of chronic back pain may be most relevant to patients making a return visit for additional care following the initial visit. The difference in the distribution of baseline risk scores between the two populations serves also to emphasise the generalisability of the score itself. In the UK population, five patients were pain-free on the Chronic Pain Grade at baseline, despite having recently consulted for back pain. However, repeating the analyses excluding these patients made no difference to the results presented here. Overall, our findings suggest that the proposed approach can be generalised to other populations even when they have a different risk spectrum.

This work demonstrates the generalisability of a prognostic approach to defining chronic pain, and in particular demonstrates a high level of reliability for the classification of people at high risk (over 80% probability) of clinically significant back pain at follow-up. This approach is likely to be appropriate for other primary care back pain populations and may be generalisable to other pain conditions, but would require further testing in other populations, notably persons 60 years and over. It is also possible that the current method could be improved as only a limited selection of prognostic factors is included. Further research testing of other prognostic variables in the calculation of a prognostic risk score may improve our assessment of chronic pain. In particular, integration of ‘yellow-flag’ risk indicators with a prognostic approach to defining chronic back pain may yield a clinically useful approach to evaluating back pain patients in primary care settings.

Acknowledgements

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Pseudo- and radicular low-back pain – A disease continuum rather than different entities? Answers from quantitative sensory testing

Rainer Freynhagen a,1, Roman Rolke b,c,*,1, Ralf Baron d, Thomas R. Tölle e, Ann-Kathrein Rutjes a, Stefan Schü f, Rolf-Detlef Treede b

a Department of Anesthesiology, Heinrich-Heine-University of Düsseldorf, Düsseldorf, Germany
b Institute of Physiology and Pathophysiology, University of Mainz, Germany
c Department of Neurology, University of Mainz, Germany
d Division of Neurological Pain Research and Therapy, Department of Neurology, University of Kiel, Germany
e Department of Neurology, Technische Universität München, Germany
f Department of Neurosurgery, Heinrich-Heine-University of Düsseldorf, Düsseldorf, Germany

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Abstract

To assess whether pseudoradicular low-back pain may be associated with subclinical sensory deficits in the distal extremity, we applied the quantitative sensory testing protocol of the German Research Network on Neuropathic Pain (DFNS) in 15 patients with pseudoradicular pain distribution. Sixteen age- and gender-matched healthy control subjects as well as 12 patients with radicular pain syndromes (L4-S1) were studied with the same protocol. Radicular pain was diagnosed using clinical criteria (pain radiation beyond the knee, motor-, sensory-, or reflex deficits, positive Lasègue’s test). Z-score QST profiles revealed a selective loss of vibration detection, detection of v. Frey hair contact, and cold detection in the affected dermatomes in the radicular pain group. The contralateral dermatome was also affected, but to a lesser degree. In patients with pseudoradicular pain, the sensory profile was similar, but sensory loss was less pronounced than in the radicular pain patients. There was no significant difference between the two patient groups. Vibration detection was the most sensitive parameter with 73% abnormal values in radicular and 47% in pseudoradicular cases. These data verified the sensitivity of QST to detect sensory loss in radicular compression syndromes, and support a neuropathic component in low-back pain with radiculopathy. In contrast to some central pain syndromes this sensory loss involved predominantly large fiber functions. The subclinical sensory loss in pseudoradicular cases suggests that these patients may also have a neuropathic component of their chronic pain. The spatial incongruence of pain and sensory loss in pseudoradicular pain, however, may also indicate that the two are not causally related.

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Keywords: Neuropathic pain; Mixed pain; Quantitative sensory testing; QST; Radiculopathy; Pseudoradiculopathy

Abbreviations: DMA, dynamic mechanical allodynia; CDT, cold detection threshold; CPT, cold pain threshold; DFNS, Deutscher Forschungsverbund Neuropathischer Schmerz = German Research Network on Neuropathic Pain; HPT, heat pain threshold; MDT, mechanical detection threshold; MPS, mechanical pain sensitivity; MPT, mechanical pain threshold; PHS, paradoxical heat sensation; PPT, pressure pain threshold; QST, quantitative sensory testing; TSL, thermal sensory limen; VDT, vibration detection threshold; WDT, warm detection threshold; WUR, wind-up ratio.

* Corresponding author. Address: Department of Neurology, Johannes Gutenberg-University, Langenbeckstr. 1, 55131 Mainz, Germany. Tel.: +49 6131 170; fax: +49 6131 175570.
E-mail address: rolke@uni-mainz.de (R. Rolke).

1 Authors contributed equally.

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1. Introduction

Pain that radiates distally at the extremities is clinically divided into radicular and pseudoradicular syndromes. Radicular pain is defined as a pain that radiates below the knee whereas pseudoradicular pain does not cross this border (Bruegger, 1960; Sutter, 1974; Wall and Melzack, 1999). The rationale behind this distinction stems from the hypothesis that pain from local proximal disorders that do not affect any nerves or nerve roots, i.e. facet joint affection, piriformis syndrome, might be perceived in proximal dermatomes within the thigh (referred pain, head zones), whereas pain from disorders associated with nerve root compression often is felt in distal dermatomes below the knee (projected pain). This distinction is thought to be clinically relevant since a projected pain always involves a damage or irritation of peripheral nerves or nerve roots, i.e. has a neuropathic component, whereas referred pain occurs without nerve involvement and might therefore be purely nociceptive. Furthermore, this distinction is thought to be therapy-relevant since neuropathic and nociceptive pain require different therapeutical strategies. Although both types of pain respond to several drugs such as opioids, nociceptive pain is sensitive to NSAIDs, whereas neuropathic pain is predominantly sensitive to antidepressants and anticonvulsants (Dworkin et al., 2003; Finnerup and Jensen, 2006).

In addition to clinical bedside examination (e.g. tendon reflexes, sensory and motor function, Lasegue’s test: pain upon straight leg raise), radiological exams and neurophysiological testing are often used to determine a nerve lesion or nerve compression in these patients and to document the radicular component. These approaches might, however, be inconclusive due to several reasons: the clinical relevance of various radiological “abnormal” findings in the lumbar spine is controversial as previous studies have shown that abnormalities in radiological exams poorly correlate with clinical symptoms (Wiesel et al., 1984; Jensen et al., 1994; Weishaupt et al., 1998; Beattie et al., 2000; Kjaer et al., 2005). Furthermore, nerve fibers involved in the conduction of pain are in particular small afferent nerve fibers (c-fibers). However, the neurophysiologic armamentarium of conventional sensory nerve conduction only tests the large fiber function (myelinated Aα fibers, Aβ fibers), thus, a deficit in small fiber function might escape this assessment (Cruccu et al., 2004). This gap can be bridged by using psychophysical methods like Quantitative Sensory Testing (QST) or neurophysiological techniques like Laser-evoked potentials (Quante et al., 2003). QST is a reliable psychophysical test of large- and small-fiber sensory modalities with a reproducibility comparable to that of nerve conduction studies (Zwart and Sand, 2002; Bird et al., 2006). QST permits a differential assessment of preserved sensation and subclinical deficit and may therefore have the potential to improve our pathophysiological understanding of radicular and pseudoradicular syndromes.

The purpose of this study was to investigate whether the distinction between radicular and pseudoradicular pain is really substantial and clinically relevant or whether it is possible to detect subtle radicular symptoms even in so-called “pseudoradicular” patients. The questions in detail were:

(1) Is it possible to detect radicular sensory deficits in distal dermatomes in pseudoradicular patients using sensitive measures of somatosensory function (quantitative sensory testing, small and large fiber function)?
(2) If yes, do patients that have been classified clinically as having pseudo- or radicular pain differ concerning their somatosensory profile in distal dermatomes?

2. Materials and methods

The study was purely observational, and there were no recommendations for additional diagnostic measures or interventions. Pain management was not delayed or altered by participation in this study. The QST protocol and consent forms were reviewed and approved by the Ethic Committees of all participating centers in accordance with the ethical principles originating from the Declaration of Helsinki and in compliance with Good Clinical Practice.

2.1. Study population

Thirty patients with chronic low-back pain radiating into parts of one leg were evaluated for this study. Exclusion criteria were other neurological diseases, diabetes and the inability to understand the instructions of the QST-battery. Patients were classified independently by four independent experienced clinicians (one pain medical specialist, two neurologists, one neurosurgeon) who determined the predominant pain type (radiculopathy vs. pseudoradiculopathy) by means of clinical characteristics derived from neurological bedside examination, pain drawings and using whatever diagnostic methods were considered appropriate (imaging, electrophysiology, etc.). Criteria for radicular pain were: typical dermatomal pain radiating beyond the knee towards the foot (reported by the patient verbally and using pain drawings), pain evoked by stretching of the femoral nerve, signs of nerve root dysfunctions such as sensory impairment, motor symptoms from compression of one lumbar nerve root (L4, L5, S1) and/or absent or diminished quadriceps femoris or triceps surae reflexes (Table 1). The diagnostic criteria of pseudoradiculopathy were as follows: pain pattern non-dermatomal in distribution, absence of motor signs and normal reflexes. Additionally available results of electrophysiology and imaging techniques (lumbar X-ray, computed tomography or magnetic resonance imaging) were also taken into account.
In 27 of 30 patients (90% of all patients) all four experienced clinicians had concordant judgements regarding the presence of a predominant radicular (n = 12) or pseudoradicu-
lar (n = 15) back pain. Only these 27 patients were included for further analysis. The mean age of the radicular patients was 50.6 ± 15.6 years (33.3% men), the mean age of the pseudora-
dicular patients was 54.2 ± 16.2 years (41.7% men). Sixteen healthy volunteers were used as healthy control subjects (mean age 51.6 ± 16.1 years; 43.8% men). They were age- and gender-
matched to the patient groups. Unpaired t-test revealed no sig-
nificant differences regarding age and gender between the patient groups or healthy control subjects (all p > 0.50).

Demographic patient data are shown in Table 1.

### 2.2. Quantitative sensory testing (QST)

We assessed the presence of sensory signs by QST using a comprehensive battery consisting of 7 tests measuring 13 parameters. This QST battery, assembling a list of robust and validated short form tests representing measures of all relevant submodalities of the somatosensory system, was developed as part of the nationwide multicenter German Research Network on Neuropathic Pain (for complete description see Rolke et al., 2006a; Rolke et al., 2006b). The tests contained both thermal and mechanical test stimuli, namely: thermal pain thresholds for cold and hot stimuli, thermal detection thresholds for the perception of cold, warm and paradoxical heat sensations, mechanical pain sensitivity including thresh-
olds for pinprick and blunt pressure, mechanical detection thresholds for touch and vibration, a stimulus-response-func-
tion for pinprick sensitivity and dynamic mechanical allodynia as well as pain summation to repetitive pinprick stimuli. Patients with lower back pain were assessed within the depen-
dent dermatome over ipsi- and contralateral foot dorsum. Hand dorsum ipsilateral to the most painful side of the lower back served as an intraindividual control area.

### 2.3. Z-transformation of QST data

To compare a single patient’s QST data profile with the group mean of accurately age- and gender-matched healthy controls (data from left and right body side pooled) we created profiles of sensory changes while patients’ data were z-transformed for each single parameter by using the following expression:

\[
Z\text{-score} = \frac{\text{Mean}_{\text{single patient}} - \text{Mean}_{\text{controls}}}{\text{SD}_{\text{controls}}}
\]

This procedure results in a QST profile where all parameters are presented as standard normal distributions (zero mean, unit variance). Z-values above “0” indicate a gain of function when the patient is more sensitive to the tested stimuli compared with controls (hyperalgesia, allodynia, hyperpathia), while z-scores below “0” indicate a loss of function referring to a lower sensitivity of the patient (small and large fiber functions). A z-score of zero represents a value corresponding to the group mean of the healthy control subjects. A z-score of

<table>
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<tr>
<th>Age</th>
<th>Gender</th>
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<th>Sensory deficit</th>
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</table>

AD, antidepressant; AC, anticonvulsant; MR, muscle relaxant; NSAID, non-steroidal anti-inflammatory drug; COX-2, COX-2 inhibitor.

* In pseudoradicular patients the distribution of pain was localized to the gluteal region or thigh but never below knee level.
3. Results

3.1. Clinical profile of radicular vs. pseudoradicular patients

Based on their clinical profile 27 patients were assigned to either a group of patients with radicular (n = 12) or pseudoradicular low back pain (n = 15). The patient groups showed similar intensities of ongoing pain. Radicular patients had a mean ongoing pain score of 6.4 ± 1.8 (NRS; 0–10), pseudoradicular patients of 5.3 ± 2.3 (unpaired t-test; p = 0.19). During clinical examination and as depicted from their pain drawings all radicular patients demonstrated radiating pain beyond the knee, while all pseudoradicular patients did not. Motor deficits of the leg were present only in the radicular group (in 3 of 12 patients corresponding to 25%). A majority of radicular patients demonstrated clinically a sensory deficit (6 of 12 patients corresponding to 50%), while this sign was only present in 3 of the 15 pseudoradicular patients (20%). Reflex deficits could be found in 3 out of 12 radicular patients, while this phenomenon was absent in the other group. This low number of patients in the radicular group with reflex deficits was most probably due to the larger number of cases with an L5-syndrome (in 58.3% of the patients), where such a deficit is hardly detectable. This is because the L5-related tibialis posterior reflex is frequently not triggerable – even in healthy subjects. Pain evoked by stretching of the femoral nerve was inducible in 5 of the radicular patients (42%), whereas a normal sensitivity of this nerve was found in the pseudoradicular group. For detailed demographic and clinical data, see Table 1.

3.2. Sensory profiling

Fig. 1 shows the complete sensory phenotype (sensory profiling) of the radicular and pseudoradicular patient groups over affected dermatome, contralateral foot dorsum, and hand dorsum ipsilateral to the most affected side of the lower back. Both the radicular and the pseudoradicular patients show signs of sensory loss that were graded with diameter of the responsible nerve fibers following the rule: the thicker the affected nerve fiber, the larger the amount of sensory loss (Aβ > Aδ; VDT: vibration detection thresholds > MDT: mechanical detection thresholds > CDT: cold detection thresholds). This sensory loss was gradually more pronounced in the radicular group, although there was no significant difference between the patient groups for any of the QST parameters. The small amount of dynamic mechanical allodynia (DMA) in the radicular group was due to one patient. This difference was not significant at the group level.

3.3. QST procedures show significant differences comparing patients and controls across the tested body regions

ANOVA of QST data demonstrates differences comparing patient groups and controls for CDT, TSL (thermal sensory limen, the difference threshold for alternating warm and cold stimuli), MDT, and VDT (Table 2, Table 3, Figs. 2–4) with patients less sensitive to non-painful large fiber stimuli. Additionally, ANOVA revealed differences across tested body regions (affected and contralateral foot dorsum, hand dorsum) for the same QST parameters plus PHS (the number of paradoxical heat sensations during the TSL procedure), and CPT (cold pain threshold). The significant group by region interaction terms for CDT, TSL, MDT, and VDT indicate that the sensory deficits were localized and not generalized to the entire body (Figs. 2–4): all QST mean thresholds of these Aβ and Aδ mediated stimuli were increased over the affected foot, followed by the contralateral foot, then hand dorsum, pronounced for the radicular patients followed by the pseudoradicular patients for each of these parameters. Paradoxical heat sensations (PHS) were generally more frequent at the feet (Table 3); a significantly increased number of paradoxical heat sensations was present only over the affected foot in the radicular as well as in the pseudoradicular group. For CPT, radicular patients were more sensitive at the affected dermatome than the other groups, but less sensitive at the hand, explaining the significant interaction of group and tested body
region; the main effect of body region indicates that the contralateral foot was the least sensitive region (Fig. 5).

4. Discussion

This study has shown that it is possible to detect radicular sensory deficits in distal dermatomes in pseudoradicular patients using quantitative sensory testing predominantly for large fiber functions. Although sensory deficits were more pronounced for radicular patients, these differences were not statistically significant, when compared with pseudoradicular patients. Radiating back pain is usually divided into pseudoradicular and radicular syndromes (Gross, 1977; Saal et al., 1988). The rationale behind this distinction stems from the assumption that neuropathic vs. nociceptive pain types differ concerning their underlying pain generating mechanism. In pseudoradicular low-back pain a proximal nociceptive event like mechanical factor, musculoskeletal dysfunctions, degenerative changes in connective tissues and local or even systemic inflammation are regarded to lead to a referred sensation in proximal dermatomes of the leg (nociceptive component). A convergent afferent input from deep somatic and cutaneous domains to spinothalamic tract neurons may explain this phenomenon (convergence–projection theory). In contrast, compression or damage to a nerve root by a protruded intervertebral disc or an inflammatory etiology (e.g. leakage of inflammatory substances from the ruptured nucleus pulposus) are suspected to be the main causes of radicular pain which is therefore categorized as pain with a neuropathic component. In these patients.
the dermatomal distribution of the pain even in areas below the knee is explained by a projected pain sensation due to the proximal affection of nerve roots. Because of the assumed pathogenetic differences the distinction is thought to be clinically and therapeutically relevant.

In the current study, we demonstrated subclinical sensory deficits in the pseudoradicular low-back pain group using QST. This raises the question, whether it is really appropriate to draw a clear line between radicular and pseudoradicular patients, or whether pseudoradicular syndromes indicate a milder degree of nerve root damage by not affecting all nerve fibers in the root. In this case, pseudoradicular low-back pain might also require treatment strategies to address neuropathic pain. This suggestion has to be tested by appropriate therapeutic trials.

4.1. Somatosensory profiles in pseudoradicular and radicular low-back pain

We verified the sensitivity of QST to document sensory loss in radiculopathy. In addition we documented subclinical sensory loss in pseudoradiculopathy. On the basis of clinical characteristics and all available diagnostic methods which were considered appropriate, four experienced pain specialists independent of each other made coincident judgements regarding the presence of a predominant radicular or pseudoradicular back pain in 90% of all patients (Table 1). Because of this clear clinical distinction one might expect clear differences in the somatosensory phenotype of patients, the pseudoradicular group having no sensory disturbances. Surprisingly, however, we detected a profound sensory loss not only in patients with typical clinical radicular symptoms but also in those with pseudoradiculopathy. Our QST data demonstrate clear evidence for subclinical sensory deficits in the distal L5 dermatome also in pseudoradicular syndromes.

In the radicular group, the sensory deficit and the pain distribution were present in the same dermatomal area, both areas were congruent. This congruence provides strong evidence that a neuropathic component contributes to the pain. Interestingly, no sensory loss was found for afferents in the C-fiber range. This observation differs from some central pain syndromes (Boivie et al., 1989) and implies that a central disinhibition process due to loss of A-fiber input might be involved in pain generation. In the pseudoradicular group, however, the pain radiation and the sensory deficit demonstrated by QST were not congruent: the pain was not felt in the foot. This finding might indicate that, although a subclinical neuropathy is clearly present, the pain is not of neuropathic origin. Alternatively, one could hypothesize that a mild root compression might damage only a subset of nociceptive C-fibers, i.e. fibers projecting to proximal areas of the dermatome, leaving the distal C-fibers intact, whereas a damage of all A-fibers in the root which are more susceptible to pressure leads to the distal sensory loss. However, so far there is no evidence for such an outer-inner somatotopy within nerve roots.

Extrapolated to daily clinical practice one should consider that patients although clearly classified as having pseudoradicular symptoms may suffer from a clinically unapparent nerve fiber damage. Reasons are manifold. Previous experimental and clinical studies have elucidated biochemical interactions between affected disc tissue and nerve roots and demonstrated that inflammatory mediators can affect fibers in nerve roots at the same or neighbouring segments without mechanical compression (Gronblad et al., 1994; Coppes MH et al., 1997; Peng et al., 2005a; Peng et al., 2005b). Another study recently demonstrated the effect of cyclic mechanical stress on the production of inflammatory

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Table 2

Analysis of variance comparing z-score sensory profiles of patients with low back pain over different body areas

<table>
<thead>
<tr>
<th>QST parameter</th>
<th>Patient groups/controls</th>
<th>Body region</th>
<th>Interaction group by region</th>
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<tr>
<td>MDT</td>
<td>15.5</td>
<td>&lt;0.001</td>
<td>9.6</td>
</tr>
<tr>
<td>VDT</td>
<td>9.1</td>
<td>&lt;0.001</td>
<td>20.6</td>
</tr>
<tr>
<td>DMA</td>
<td>2.5</td>
<td>n.s.</td>
<td>1.5</td>
</tr>
<tr>
<td>PHS</td>
<td>1.1*</td>
<td>n.s.</td>
<td>5.4</td>
</tr>
</tbody>
</table>

n.s., not significant (p > 0.05).

* This is the highest non-significant F-value, corresponding to p = 0.06.
### Table 3
Quantitative sensory testing

<table>
<thead>
<tr>
<th>QST parameter</th>
<th>Affected foot</th>
<th>Contralateral foot</th>
<th>Hand</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Radicular</td>
<td>Pseudoradicular</td>
<td>Control</td>
</tr>
<tr>
<td><strong>CDT (°C)</strong></td>
<td>0.927 ± 0.294</td>
<td>0.870 ± 0.347</td>
<td>0.428 ± 0.280</td>
</tr>
<tr>
<td><strong>WDT (°C)</strong></td>
<td>0.914 ± 0.197</td>
<td>0.947 ± 0.226</td>
<td>0.785 ± 0.236</td>
</tr>
<tr>
<td><strong>TSL (°C)</strong></td>
<td>1.159 ± 0.301</td>
<td>1.234 ± 0.269</td>
<td>0.993 ± 0.230</td>
</tr>
<tr>
<td><strong>CPT (°C)</strong></td>
<td><strong>HPT (°C)</strong></td>
<td><strong>PPT (kPa)</strong></td>
<td><strong>MPT (mN)</strong></td>
</tr>
<tr>
<td><strong>PPT (kPa)</strong></td>
<td>2.674 ± 0.151</td>
<td>2.716 ± 0.200</td>
<td>2.712 ± 0.159</td>
</tr>
<tr>
<td><strong>MPT (mN)</strong></td>
<td>1.495 ± 0.318</td>
<td>1.397 ± 0.512</td>
<td>1.389 ± 0.363</td>
</tr>
<tr>
<td><strong>MPS (rating 0–100)</strong></td>
<td>0.327 ± 0.732</td>
<td>0.340 ± 0.268</td>
<td>0.309 ± 0.141</td>
</tr>
<tr>
<td><strong>WUR (ratio)</strong></td>
<td>0.241 ± 0.238</td>
<td>0.340 ± 0.268</td>
<td>0.309 ± 0.141</td>
</tr>
<tr>
<td><strong>MDT (mN)</strong></td>
<td>1.202 ± 0.548</td>
<td>0.839 ± 0.524</td>
<td>0.319 ± 0.298</td>
</tr>
<tr>
<td><strong>VDT (x/8)</strong></td>
<td>0.792 ± 0.722</td>
<td>0.793 ± 0.716</td>
<td>0.793 ± 0.716</td>
</tr>
<tr>
<td><strong>DMA (rating 0–100)</strong></td>
<td>0.793 ± 0.716</td>
<td>0.793 ± 0.716</td>
<td>0.793 ± 0.716</td>
</tr>
<tr>
<td><strong>PHS (x/3)</strong></td>
<td>1.4 ± 1.4</td>
<td>1.4 ± 1.4</td>
<td>1.4 ± 1.4</td>
</tr>
</tbody>
</table>

CDT, cold detection threshold; WDT, warm detection threshold; TSL, thermal sensory limen; CPT, cold pain threshold; HPT, heat pain threshold; PPT, pressure pain threshold; MPT, mechanical pain threshold; MPS, mechanical pain sensitivity; WUR, wind-up ratio; MDT, mechanical detection threshold; VDT, vibration detection threshold; DMA, dynamic mechanical allodynia; PHS, paradoxical heat sensations. All data are presented as means ± SD.

*a* For CDT and WDT, differences from baseline-temperature (32 °C) are shown.

*b* Retransformed mean for log-normally distributed data. In the case of PHS, CPT, HPT and VDT, mean original data ± SD are shown.
agents and postulated a possible synergistic effect of simultaneous mechanical and chemical irritation of the anulus fibrosus cells on the production of pain mediators (PGE2) (Miyamoto and Nishida, 2006). This inflammatory attack of nerve roots by mediators diffusing from the damaged disc nicely explains the contralateral sensory deficits that we detected in both groups of patients.

The term “mixed pain” was established to refer to those cases of sciatica pain that may have both an inflammatory and a neuropathic component. Consistent with former findings (Hassan et al., 2004; Freynhagen et al., 2006b) a recent study with the PainDetect questionnaire in approximately 8,000 chronic low-back pain patients suggested a high prevalence of subjects with a predominant neuropathic pain component (37%) and

![Fig. 2. Cold detection thresholds of pseudoradicular and radicular patients compared with healthy controls. Radicular (filled symbols) more than pseudoradicular patients (semifilled symbols) showed increased cold detection thresholds (CDT) over the affected foot more pronounced than over the contralateral foot when compared with controls (open symbols). Both patient groups did not show any significant difference when comparing each other. No differences for both patient groups and controls could be found comparing CDT over hand dorsum. Shown data represent mean thresholds ± SEM.](image)

![Fig. 3. Mechanical detection thresholds of pseudoradicular and radicular patients compared with healthy controls. Radicular (filled symbols) more than pseudoradicular patients (semifilled symbols) showed increased mechanical detection thresholds (MDT) over the affected foot more pronounced than over the contralateral foot when compared with controls (open symbols). Both patient groups did not show any significant difference when comparing each other. Only the radicular patients showed higher MDT values over hand dorsum compared with controls. Shown data represent mean thresholds ± SEM.](image)

![Fig. 4. Vibration detection thresholds of pseudoradicular and radicular patients compared with healthy controls. Radicular (filled symbols) more than pseudoradicular patients (semifilled symbols) showed increased vibration detection thresholds (VDT) over the affected foot more pronounced than over the contralateral foot when compared with controls (open symbols). Both patient groups did not show any significant difference when comparing each other. Only the radicular patients showed higher VDT values over hand dorsum compared with controls. Shown data represent mean thresholds ± SEM.](image)

![Fig. 5. Cold pain thresholds of pseudoradicular and radicular patients compared with healthy controls. Radicular patients (filled symbols), pseudoradicular patients (semifilled symbols), and control subjects (open symbols) never differ significantly within each tested body region. However, this figure shows a significant interaction of test group and body region, since cold pain thresholds of radicular patients differ across different body regions. Shown data represent mean thresholds ± SEM.](image)
identified at the same time 28% of patients with mixed pain (Freyenhagen et al., 2006a).

The pattern of decreased perception suggests a predominant damage of myelinated fibers projecting to the lower limb. Unmyelinated fibers were not significantly affected in both groups. This finding is consistent with experimental nerve compression studies showing that tactile Aβ-fibers are blocked first, followed by Aδ- and cold-fibers, then nociceptive Aδ-fibers, and finally C-fibers (Ziegler et al., 1999). Accordingly, it was shown that myelinated nerve fibers are the first to be damaged as a result of nerve root compression (Yoshizawa et al., 1995) usually caused when a herniated disc irritates or compresses nerve roots in the lower spine. However, in advanced cases also unmyelinated fibers are affected (Nygaard and Mellgren, 1998; Yamashita et al., 2002).

4.2. Control groups

In order to validate our QST findings as precisely as possible we compared the somatosensory profiles of our patients with two different groups of healthy controls. Within our study 16 volunteers served as accurately age- and gender-matched control subjects (see Section 2.1). Furthermore, we compared our data with age- and gender-matched subjects from the German Research Network on Neuropathic Pain (DFNS) reference database (Rolke et al., 2006a). This population-based reference database consists of 180 healthy phenotypically completely characterized human subjects measured with a standardized QST battery that consists of 7 tests measuring 13 parameters obtained for 3 body regions. The comparison of our data with both reference groups confirmed our findings in either case. For the tested QST parameters it can statistically be expected that 5% of the QST values from healthy control subjects range outside the reference range (95% confidence interval of the independent DFNS QST-database (Rolke et al., 2006a). Accordingly, the QST values from the age- and gender-matched control group (n = 16) from the present study met exactly these expectations with 4.6% of QST values ranging outside the reference range of the DFNS QST-database. In contrast 28.0% of the QST values from radicular, and 20.5% of the QST values from pseudoradiculic patients showed pathological values outside the DFNS reference range. For pseudoradiculic patients 40% of CDT, 6.7% of MDT, and 46.7% of VDT values were increased compared to DFNS reference data. This increase was more pronounced for the radicular patients with 36.4% of CDT, 45.5% of MDT, and 72.7% of VDT values outside the reference range.

4.3. Possible consequences for clinical practice

Our data using a standardized quantitative sensory testing protocol suggest that the symptoms and signs of either pseudo-radiculopathy or radiculopathy patients reflect more of a disease continuum rather than different disease entities. Treatment effects in the radicular group may have contributed to the unexpected similarity of the two patient groups. The spatial incongruence of pain and sensory deficit in pseudoradicular pain leaves some doubt about the neuropathic nature of the pain in these patients. If, however, in fact many low-back pain patients with pseudoradicular syndromes suffer from an unrecognized neuropathic pain component, we may need to re-think our current therapeutic and diagnostic strategies, since neuropathic pain requires a different first-line treatment approach (Dworkin et al., 2003; Finnerup et al., 2005). The available evidence suggests that in these cases antidepressants and/or anticonvulsants in combination with either opioids, traditional nonsteroidal anti-inflammatory drugs or muscle relaxants could be useful (Moskowitz, 2003; Baron and Binder, 2004; Finnerup et al., 2005). Prospective treatment studies are needed before one can make firm conclusions about treating pseudoradicular and radicular pain identically or differently.

Acknowledgement

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References


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A systematic literature review of psychological factors and the development of late whiplash syndrome

Esther Williamson *, Mark Williams, Simon Gates, Sarah E. Lamb

University of Warwick, Clinical Trials Unit, Room B169 Medical School Building, Gibbert Hill Campus, CV4 7AL Coventry, United Kingdom

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Abstract

This systematic literature review aims to assess the prognostic value of psychological factors in the development of late whiplash syndrome (LWS). We included prospective cohort studies that provided a baseline measure of at least one psychological variable and used outcome measures relating to LWS (i.e. pain or disability persisting 6 months post injury). A search of electronic databases (Pubmed, Medline, Cinahl, Embase and Psychinfo) up to August 2006 was done using a predetermined search strategy. Methodological quality was assessed independently by two assessors. Data extraction were carried out using a standardised data extraction form. Twenty-five articles representing data from 17 cohorts were included. Fourteen articles were rated as low quality with 11 rated as adequate quality. Meta-analysis was not undertaken due to the heterogeneity of prognostic factors, outcome measures and methods used. Results were tabulated and predefined criterion applied to rate the overall strength of evidence for associations between psychological factors and LWS. Data on 21 possible psychological risk factors were included. The majority of findings were inconclusive. Limited evidence was found to support an association between lower self-efficacy and greater post-traumatic stress with the development of LWS. No association was found between the development of LWS and personality traits, general psychological distress, wellbeing, social support, life control and psychosocial work factors. The lack of conclusive findings and poor methodological quality of the studies reviewed highlights the need for better quality research. Self-efficacy and post-traumatic distress may be associated with the development of LWS but this needs further investigation.

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Keywords: Late whiplash syndrome; Prognosis; Psychological factors

1. Introduction

The Quebec Task Force (Spitzer et al., 1995) defined late whiplash syndrome (LWS) as the presence of pain, restriction of motion or other symptoms six months or more after a whiplash injury, sufficient to hinder return to normal activities such as driving, usual occupation and leisure. LWS is reported in between 16% (Pennie and Agambar, 1991) and 71% (Karlsborg et al., 1997) of people experiencing a whiplash injury, and represents a significant public health problem worldwide. The overall cost of whiplash injuries to the UK economy is estimated at £2553 million each year (1990 prices) with a considerable amount of the costs related to those who develop long-term problems (Galasko, 1998).

There are many factors that might contribute to the development of LWS. Previous reviews have concluded that collision characteristics are not involved (Scholten-Peeters et al., 2003). The role of age and gender is unclear (Cote et al., 2001; Scholten-Peeters et al., 2003) but initial pain intensity is a strong and consistently reported predictor. More recently, considerable attention has been paid to the potential role of psychological factors. Psychological variables are implicated in

* Corresponding author. Tel.: +44 (0) 24 765 74650.
E-mail address: e.m.williamson@warwick.ac.uk (E. Williamson).

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the development of long-term disability in low back pain (LBP) (Pincus et al., 2002) and similar mechanisms may act in LWS.

The identification of prognostic factors has implications for patient management. First, it would facilitate the screening of patients to identify those at risk of developing LWS. Second, it would help to guide patient management by identifying factors that can potentially be modified to improve outcomes. Research investigating treatment regimes has proved to be largely inconclusive (Verhagen et al., 2004) so identifying factors that influence outcome might allow the development of more effective strategies.

An earlier review by Scholten-Peeters et al. (2003) which included literature up to April 2002 reported on the limited research that was available regarding psychological factors. This review included psychological constructs such as acute psychological response to injury, previous psychological problems, stress unrelated to the injury, personality traits and cognitive function. The findings of this review were largely inconclusive but there was limited evidence that previous psychological problems and nervousness were predictive of poor outcome. Nervousness was measured using the nervousness scale of the Freiburg Personality Inventory, which is thought to reflect a tendency to report psychosomatic symptoms (Radanov et al., 1994a). High acute psychological response to the injury was not found to be a prognostic factor.

The literature has expanded with 13 articles reporting 11 cohorts being published since this earlier review. The range of psychological factors under investigation has diversified including health behaviour, beliefs about pain, distress, depression, anxiety and ability to cope. In view of new developments in this area a systematic review of the literature is needed. This review aims to provide a comprehensive and up to date review of psychological risk factors for the development of LWS.

2. Methods

2.1. Search strategy

Searches were carried out using an electronic search strategy outlined in Fig. 1. Searches covered databases from their start to August 2006.

Articles were eligible for this review if they fulfilled the following criteria: prospective or population-based cohort studies or case-control studies investigating prognostic factors and the development of LWS; prognostic factors studied included a measurement of at least one psychological variable at baseline; cohort was assembled within 6 weeks of injury; 6 months minimum follow up; outcome measures used related to the clinical presentation of LWS (e.g. pain or disability due to neck problems 6 months post injury); English language. Studies were

Pubmed, Medline, CINAHL, Embase and Psych Info were searched using the following terms:

"Whiplash Injuries" (MeSH term), "whiplash", "whiplash associated disorders", "neck strain" or "neck sprain" combined with "prognosis", "outcome", "recovery", "cohort study", "follow-up study", "prospective" and "observational".

3078 articles identified. Duplicates removed.
Abstracts were screened using the inclusion and exclusion criteria.

7 potential articles were identified in non-English languages
- The cohort was reported in an English version = 3
- Potentially eligible = 4 but ineligible due to language

108 articles appeared to fulfill the inclusion and exclusion criteria.
In addition, reference lists were searched but revealed no new articles.

83 articles were excluded as they did not fulfill the inclusion and exclusion criteria.
This included 20 articles that were prospective studies but did not measure any psychological factors.

25 articles reporting 17 cohorts pertaining to "psychological" factors were included in this review.

Fig. 1. Search strategy.
excluded if they were pertaining to neck pain other than that arising from a whiplash injury or if the outcome measure used did not relate to the development of LWS e.g. “time to claim closure”. Factors were considered to be “psychological” if they were related to the mental or emotional state of a person (Pearlsall, 1998). This included measures of constructs such as cognition, anxiety, depression, distress, beliefs and coping. This is a similar approach to that taken by Pincus et al. (2002) in their review of psychological prognostic factors for LBP.

2.2. Data extraction and quality assessment

Data extraction and quality assessments were carried out by the four authors. Each article was assessed and had data extracted by two authors independently. Four articles were assessed and data extraction carried out by all 4 authors to establish consistency in the procedure. Data extraction were carried out using a standardised data extraction form and included the study characteristics (e.g. population, sample size, length of follow up), outcome measures and prognostic factors studied and results of the studies. Following independent data extraction the completed forms were compared and any discrepancies were resolved by discussion amongst the four authors. Similarly, the quality assessment of the 25 eligible articles was also carried out by 2 reviewers who assessed the studies independently using a quality assessment tool based on recommendations by Altman (1991) (Supplementary Table 1).

The quality scoring was divided into three sections: patient sampling, measurements used and analysis. In the analysis section points were awarded if multivariate analysis was used as this is necessary in observational studies to attempt to reduce bias. Many variables could be controlled for but 4 factors were specified as being essential when analysing relationships between prognostic factors and outcome in this patient group. These were initial pain severity, age, gender and history of previous neck pain. Initial pain intensity is consistently reported as a strong predictive factor (Cote et al., 2001; Scholten-Peeters et al., 2003). There is conflicting evidence regarding gender and age and their influence on recovery following a whiplash injury (Cote et al., 2001; Scholten-Peeters et al., 2003). There is conflicting evidence regarding gender and age and their influence on recovery following a whiplash injury (Cote et al., 2001; Scholten-Peeters et al., 2003). However, differences in pain perception are thought to exist between male and females (Rollman et al., 2004) so could potentially influence recovery. Biomechanical changes associated with ageing may also affect capacity for recovery (Adams and Dolan, 2005). A history of previous neck pain may also influence pain perception due to changes that occur in the nervous system in the presence of pain (Coderre et al., 1993) resulting in greater pain intensity reported by this patient subgroup leading to poorer outcomes.

Any discrepancies in quality assessment were resolved by discussion and any remaining disagreements were referred to a third party (another author of this review) for adjudication. An overall quality score was then assigned to each article. Rather than using the total score as a cut off for deciding quality ratings, we used the scores of each section. Each section was of equal importance and this needed to be reflected in the quality rating. This was to prevent articles that scored very highly in one section but very poorly in others gaining a rating that may not reflect the overall methodological quality. Each article was graded as a high, adequate or low quality study according to the following definitions:

- High quality = scored 75% or above for all three sections.
- Adequate quality = scored at least 50% for all three sections.
- Low quality = scored less than 50% for any one section.

2.3. Evidence synthesis

The results were collated into a table to allow the comparison of results and to assess overall levels of evidence for each prognostic factor. Meta-analysis was not possible due to the variability in the prognostic factors and outcome measures. There were 21 different psychological factors investigated but even similar constructs were measured in different ways and the studies used different outcome measures. For example personality traits were measured using the Temperament and Character Inventory, Eysenck Personality Inventory-1, Frieburg Personality Inventory and the Millon Clinical Multiaxial Inventory. Outcome measures used also varied greatly between studies. Studies also failed to report effect sizes and measures of variability that are necessary for meta-analysis.

The overall levels of evidence for each risk factor were defined as strong, moderate, limited and inconclusive according to the definitions below. These definitions do not reflect the strength of association found between the prognostic factor and the development of LWS but identifies how often an association was seen based on a statistically significant association being reported. This is a similar approach used by other systematic reviews (Scholten-Peeters et al., 2003). This approach could potentially be biased when the results from one cohort are published in more than one article but this was taken into consideration in the definitions below.

- Strong evidence: consistent findings from at least 2 high quality articles from different cohorts.
- Moderate evidence: consistent findings in at least 2 adequate quality articles from different cohorts.
- Limited evidence: findings in one adequate quality article or at least 2 low quality articles from different cohorts.
- Inconclusive evidence: Inconsistent findings or insufficient research (e.g. evidence from one low quality cohort only).

3. Results

3.1. Study characteristics

This review included 25 articles reporting data from 17 cohorts. The studies included in the review are presented in Table 2. This summarises the prognostic factors investigated. The majority of studies recruited patients from Emergency Department settings (n = 11 cohorts, 12 articles). There was one cohort (7 articles) that recruited patients from a General Practice setting with two recruiting patients from both an Emergency Department and General Practice (3 articles). The remaining cohorts were based on subjects from orthopaedic departments (2 cohorts, 2 articles) and insurance
<table>
<thead>
<tr>
<th>Cohort number</th>
<th>Author(s)</th>
<th>Type of study</th>
<th>Population studied</th>
<th>Number of subjects*</th>
<th>Length of follow up</th>
<th>Psychological factors studied</th>
<th>Other prognostic factors studied</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Nederhand et al. (2004)</td>
<td>Prospective cohort</td>
<td>Emergency department</td>
<td>82/90</td>
<td>6 months</td>
<td>Fear avoidance (TSK), catastrophising (PCL-E)</td>
<td>Gender, age, collision direction, functional status, EMG, disability (NDI), pain intensity (VAS)</td>
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<tr>
<td>2</td>
<td>Olsson et al. (2002)</td>
<td>Prospective cohort</td>
<td>Emergency department</td>
<td>123/130</td>
<td>1 year</td>
<td>Psychological response to pain (MPI)</td>
<td>Pain intensity, age, sex, condition severity (WAD grade)</td>
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<tr>
<td>3</td>
<td>Kyhlback et al. (2002)</td>
<td>Prospective cohort</td>
<td>Orthopaedic department</td>
<td>83/98</td>
<td>1 year</td>
<td>Self-efficacy (SES)</td>
<td>Disability (PDI), pain intensity (VAS), age, WAD grade, gender</td>
</tr>
<tr>
<td>4</td>
<td>Hendriks et al. (2005)</td>
<td>Prospective cohort</td>
<td>General practice and emergency department</td>
<td>119/125</td>
<td>1 year</td>
<td>Psychological symptoms (SCL-90)</td>
<td>Age, gender, education, marital status, crash related factors, pre-existing health factors, pain medication, neck range of movement (ROM), neck pain intensity, number of complaints, ability to perform ADL, radicular complaints, work activities, absent from work, diagnostic imaging, use of collar</td>
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<td>Pettersson et al. (2004)</td>
<td>Case control</td>
<td>Orthopaedic department</td>
<td>39/40</td>
<td>2 years</td>
<td>Personality (TCI)</td>
<td>Age</td>
</tr>
<tr>
<td>6</td>
<td>Soderlund et al. (2000)</td>
<td>Prospective cohort</td>
<td>Emergency department</td>
<td>53/59</td>
<td>6 months</td>
<td>Coping (CSQ), self-efficacy (SES)</td>
<td>Disability (PDI)</td>
</tr>
<tr>
<td>7</td>
<td>Mattinen et al. (2004)</td>
<td>Prospective cohort</td>
<td>Insurance company records</td>
<td>144/312</td>
<td>3 years</td>
<td>Psychological status (GHQ-12), depression (BDI)</td>
<td>Symptoms, disability (NDI), ability to work, previous symptoms, crash characteristics</td>
</tr>
<tr>
<td>8</td>
<td>Sterling et al. (2005)</td>
<td>Prospective cohort</td>
<td>Emergency department</td>
<td>76/80</td>
<td>6 months</td>
<td>Psychological distress (IES), psychological state (GHQ-23), fear avoidance (TSK)</td>
<td>Neck ROM, proprioception, EMG, pressure pain thresholds, thermal pain thresholds, brachial plexus provocation test, sympathetic function, disability (NDI), pain intensity (VAS), compensation</td>
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<td>9</td>
<td>Borchgrevink et al. (1997)</td>
<td>Prospective cohort</td>
<td>Emergency department</td>
<td>88/99</td>
<td>6 months</td>
<td>Personality (MCMI-1)</td>
<td>Neck ROM, symptom severity</td>
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<tr>
<td>10</td>
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<td>Prospective cohort</td>
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<td>50/50</td>
<td>2 years</td>
<td>Psychological state (GHQ-12)</td>
<td>Gender, age, initial physical symptoms, drive/passenger status, compensation</td>
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<tr>
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<td>Mayou and Bryant (1996)</td>
<td>Prospective cohort</td>
<td>Emergency department</td>
<td>57/63</td>
<td>1 year</td>
<td>Psychological factors (BDI, SAS, EPI), previous psychological problems</td>
<td>Gender, compensation</td>
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<tr>
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<td>Mayou and Bryant (2002)</td>
<td>Prospective cohort</td>
<td>Emergency department</td>
<td>187/278</td>
<td>1 year</td>
<td>Prior emotional problems, perceived threat, blame, initial emotional distress, cognitive factors</td>
<td>(continued on next page)</td>
</tr>
<tr>
<td>Cohort number</td>
<td>Author</td>
<td>Type of study</td>
<td>Population studied</td>
<td>Number of subjects</td>
<td>Length of follow up</td>
<td>Psychological factors studied</td>
<td>Other prognostic factors studied</td>
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<tr>
<td>--------------</td>
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<td>---------------------</td>
<td>-----------------------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>13</td>
<td>Radanov et al. (1991)</td>
<td>Prospective cohort</td>
<td>General practice</td>
<td>78/92</td>
<td>6 months</td>
<td>Psychosocial stress, wellbeing (WBS), personality (FPI), cognitive function (CFQ, DST, CBTT, NCT, PASAT, TMT, CVLT)</td>
<td>Gender, age, educational attainment, vocational related variables, crash related variables, initial pain intensity (VAS), initial subjective complaints, neurological examination, timing of onset of symptoms, neck ROM, radiological examination, history of pre-traumatic headache, previous head trauma, previous whiplash injury, type and frequency of pre-traumatic headache, sleep disturbance</td>
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<td>Radanov et al. (1993a)</td>
<td>Prospective cohort</td>
<td></td>
<td>98/113</td>
<td>1 year</td>
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<td>Radanov et al. (1993b)</td>
<td>Prospective cohort</td>
<td></td>
<td>117/137</td>
<td>6 months</td>
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<tr>
<td></td>
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<td>Prospective cohort</td>
<td></td>
<td>117/137</td>
<td>6 months</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Radanov et al. (1994b)</td>
<td>Prospective cohort</td>
<td></td>
<td>117/137</td>
<td>6 months</td>
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<tr>
<td></td>
<td>Di Stefano and Radanov</td>
<td>Case control</td>
<td></td>
<td>42/42</td>
<td>2 years</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Radanov et al. (1995)</td>
<td>Prospective cohort</td>
<td></td>
<td>117/137</td>
<td>2 years</td>
<td></td>
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<tr>
<td>14</td>
<td>Karlsborg et al. (1997)</td>
<td>Prospective cohort</td>
<td>Emergency department</td>
<td>34/39</td>
<td>7 months</td>
<td>Neuropsychology (SCL-90, CFS, WCST), presence of stress unrelated to the accident</td>
<td>Gender, age, WAD grade, number of symptoms at baseline, MRI results, motor provoked potentials</td>
</tr>
<tr>
<td></td>
<td>Smed (1997)</td>
<td>Prospective cohort</td>
<td></td>
<td>29/29</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>15</td>
<td>Kasch et al. (2001)</td>
<td>Prospective cohort</td>
<td>Emergency department</td>
<td>132/141</td>
<td>1 year</td>
<td>Health behaviour (MBHI)</td>
<td>Gender, age, BMI, pain severity, neurological symptoms, number of symptoms, neck ROM, work load (cervical muscles), speed difference between vehicles, compensation</td>
</tr>
<tr>
<td>16</td>
<td>Kivioja et al. (2005)</td>
<td>Prospective cohort</td>
<td>Emergency department</td>
<td>91/96</td>
<td>1 year</td>
<td>Coping (CSQ)</td>
<td>Initial pain severity, previous neck and shoulder pain, age, sex</td>
</tr>
<tr>
<td>17</td>
<td>Atherton et al. (2006)</td>
<td>Prospective cohort</td>
<td>Emergency department</td>
<td>480/765</td>
<td>1 year</td>
<td>Psychosocial work factors (WS), psychological state (GHQ), somatisation (MSPQ)</td>
<td>General health, number of GP visits in previous 12 months, previous neck pain, presence of widespread chronic pain, collision factors, initial injury severity (VAS), initial disability (NDI), number of symptoms, WAD grade, age, gender</td>
</tr>
</tbody>
</table>

TSK, tampa scale of kinesiophobia; NDI, Neck Disability Index; MPI, West Haven-Yale multidimensional pain inventory; SES, Self-efficacy Scale; TCI, Temperament and Character Inventory; GHQ-12 or 28, general health questionnaire-12 or 28; IES, Impact of Events Scale; EMG, electromyography; EPI, Eysenck Personality Inventory; WBS, wellbeing scale; DST, digital span test; NCT, number connection test; TMT, trail making test; CFQ, cognitive function scanner; MBHI, million behavioural health inventory; PCL-E, pain cognitiotn list-experimental; PDI, pain disability index; SCL-90, symptoms checklist-90; CSQ, coping strategies questionnaire; BDI, Beck Depression Inventory; MCMI-1, Million Clinical Multiaxial Inventory; SAS, Spielberg anxiety state; FPI, Friburg Personality Inventory; CBT, Cognitive behaviour therapy; TSST, Trier social stress test; CPR, counterphobic resistance; PCL-M, pain cognitiotn list-multidimensional; PASAT, paced auditory serial addition task; CVLT, California verbal learning test; WCST, Wisconsin card sorting test; MSPQ, modified somatic perceptions questionnaire; WS, Karasek’s demand-support-control.

* Number at final follow up/number recruited.
Table 6
Overall strength of evidence for psychological prognostic factors in whiplash

<table>
<thead>
<tr>
<th>Psychological factor</th>
<th>Articles supporting an association with late whiplash syndrome</th>
<th>Study quality</th>
<th>Articles failing to show an association with the development of late whiplash syndrome</th>
<th>Study quality</th>
<th>Overall level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personality traits</td>
<td>Radanov et al. (1994a) (S)</td>
<td>Low</td>
<td>Borchgrevink et al. (1997) (S)</td>
<td>Adequate</td>
<td>No association found based on moderate evidence</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Radanov et al. (1991) (S)</td>
<td>Low</td>
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<td></td>
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<td></td>
<td>Radanov et al. (1993a) (S)</td>
<td>Adequate</td>
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<td></td>
<td>Radanov et al. (1993b) (S)</td>
<td>Low</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Radanov et al. (1994a) (S)</td>
<td>Low</td>
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<td></td>
<td></td>
<td></td>
<td>Radanov et al. (1995)</td>
<td>Low</td>
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<td></td>
<td></td>
<td></td>
<td>Pettersson et al. (2004) (D)</td>
<td>Low</td>
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<td></td>
<td></td>
<td></td>
<td>Mayou and Bryant (1996) (S)</td>
<td>Low</td>
<td></td>
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<tr>
<td>General psychological distress</td>
<td>Sterling et al. (2005) (D)</td>
<td>Adequate</td>
<td>Hendriks et al. (2005) (D)</td>
<td>Adequate</td>
<td>No association found based on moderate evidence</td>
</tr>
<tr>
<td></td>
<td>Gargan et al. (1997) (S)</td>
<td>Low</td>
<td>Karlsborg et al. (1997) (S)</td>
<td>Low</td>
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<td></td>
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<td></td>
<td>Smed (1997) (S)</td>
<td>Adequate</td>
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<td></td>
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<td></td>
<td>Miettinen et al. (2004) (D)</td>
<td>Low</td>
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<td></td>
<td></td>
<td></td>
<td>Olsson et al. (2002) (S)</td>
<td>Adequate</td>
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<td></td>
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<td></td>
<td>Sterling et al. (2006) (D)</td>
<td>Adequate</td>
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<td></td>
<td></td>
<td></td>
<td>Atherton et al. (2006) (S)</td>
<td>Adequate</td>
<td></td>
</tr>
<tr>
<td>Self-efficacy</td>
<td>Kyhlback et al. (2002) (S and D)</td>
<td>Adequate</td>
<td>Limited evidence for an association with the development of LWS</td>
<td></td>
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<tr>
<td></td>
<td>Soderlund et al. (2000) (S)</td>
<td>Low</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Post-traumatic stress</td>
<td>Sterling et al. (2005) (D)</td>
<td>Adequate</td>
<td>Limited evidence for an association with the development of LWS</td>
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<td></td>
<td>Sterling et al. (2006) (D)</td>
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<td>Psychosocial work factors</td>
<td>Physiological factors</td>
<td>Adequate</td>
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<tr>
<td></td>
<td>Atherton et al. (2006) (S)</td>
<td>Adequate</td>
<td>No association found based on limited evidence</td>
<td></td>
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<tr>
<td>Wellbeing</td>
<td>Radanov et al. (1995) (S)</td>
<td>Low</td>
<td>Radanov et al. (1991) (S)</td>
<td>Low</td>
<td>No association found based on limited evidence</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Radanov et al. (1993a) (S)</td>
<td>Low</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Radanov et al. (1993b) (S)</td>
<td>Low</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Radanov et al. (1994a) (S)</td>
<td>Low</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Di Stefano and Radanov (1995) (S)</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>Life control</td>
<td>Olsson et al. (2002) (S)</td>
<td>Adequate</td>
<td>No association found based on limited evidence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social support</td>
<td>Olsson et al. (2002) (S)</td>
<td>Adequate</td>
<td>No association found based on limited evidence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychosocial stress not related to the injury</td>
<td>Karlsborg et al. (1997) (S)</td>
<td>Low</td>
<td>Radanov et al. (1991) (S)</td>
<td>Low</td>
<td>Inconclusive</td>
</tr>
<tr>
<td></td>
<td>Smed (1997) (S)</td>
<td>Low</td>
<td>Radanov et al. (1994b) (S)</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Radanov et al. (1995)</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>Previous psychological problems</td>
<td>Mayou and Bryant (1996) (S)</td>
<td>Low</td>
<td>Mayou and Bryant (2002) (S)</td>
<td>Low</td>
<td>Inconclusive</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Radanov et al. (1991) (S)</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>Blame and anger</td>
<td>Mayou and Bryant (2002) (S)</td>
<td>Low</td>
<td>Radanov et al. (1994a) (S)</td>
<td>Low</td>
<td>Inconclusive</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Radanov et al. (1995)</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>Perceived threat</td>
<td>Mayou and Bryant (2002) (S)</td>
<td>Low</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Cognitive function</td>
<td>Radanov et al. (1991) (S)</td>
<td>Low</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Radanov et al. (1994a) (S)</td>
<td>Low</td>
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<tr>
<td></td>
<td>Radanov et al. (1994b) (S)</td>
<td>Low</td>
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<tr>
<td></td>
<td>Di Stefano and Radanov (1995)</td>
<td>Low</td>
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<tr>
<td></td>
<td>Radanov et al. (1995) (S)</td>
<td>Low</td>
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</tr>
</tbody>
</table>

(continued on next page)
company records (1 cohort, 1 article). All but two of the articles reviewed were prospective cohort articles with the remaining two being case control studies. Sample sizes ranged from 29 in a case control study (Smed, 1997) to 765 in a prospective cohort study (Atherton et al., 2006). Cohorts were most commonly followed up for 1 year \( (n = 7) \) or 6 months \( (n = 4) \) with two cohorts providing up to 3 years follow up (Miettinen et al., 2004; Sterling et al., 2006). Loss to follow up ranged from 0% (Gargan et al., 1997) to 53.9% (Miettinen et al., 2004). Mean loss to follow up was approximately 14% with 10 cohorts having less than 10% loss to follow up.

### 3.2. Methodological quality

The quality scores are recorded in Supplementary Table 3. Fifty-eight percent of articles (14 out of 25) were rated as low overall quality and the rest were rated as adequate overall quality. The majority of articles scored at least an adequate quality rating for patient sampling (>50% for this section). The biggest shortcoming in this section was that articles failed to report any treatment the cohort may have received during the course of the follow up (17 out of 25 articles). Approximately a third of articles received low quality scores for measurements used (<50% for this section) with the most problematic area being a lack of blinding of those assessing outcome to the patient’s baseline data in 20 of the articles. Fourteen articles also failed to use outcome measures with established test–retest reliability in a pain population. Articles received the lowest scores in the analysis section with only 5 articles being rated as high quality for their analysis (score >75% in this section). Sixteen articles had insufficient sample size, 11 articles did not carry out any multivariate analysis and 15 articles did not adjust for any of the specified factors of age, gender, neck pain intensity and previous neck pain.

### 3.3. The evidence

A wide range of psychological factors were reported including depression, distress, stress, anxiety, coping, self-efficacy, fear-avoidance beliefs, personality, cognitive function, history of prior psychological or emotional problems and wellbeing. Only statistically significant results have been summarised in Supplementary Tables 4 and 5. Results for factors that were not statistically significant are not reported in these tables. Borchgrevink et al. (1997) and Pettersson et al. (2004) had no significant findings and were excluded from these tables.

#### Table 6 (continued)

<table>
<thead>
<tr>
<th>Psychological factor</th>
<th>Articles supporting an association with late whiplash syndrome</th>
<th>Study quality</th>
<th>Articles failing to show an association with the development of late whiplash syndrome</th>
<th>Study quality</th>
<th>Overall level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>Radanov et al. (1995) (S)</td>
<td>Low</td>
<td>Radanov et al. (1994b) (S)</td>
<td>Low</td>
<td>Inconclusive</td>
</tr>
<tr>
<td></td>
<td>Mayou and Bryant (1996) (S)</td>
<td>Low</td>
<td>Mayou and Bryant (1996) (S)</td>
<td>Low</td>
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</tr>
<tr>
<td>Depression</td>
<td>Miettinen et al. (2004) (D)</td>
<td>Low</td>
<td>Mayou and Bryant (1996) (S)</td>
<td>Low</td>
<td>Inconclusive</td>
</tr>
<tr>
<td>Irritability</td>
<td>Radanov et al. (1995) (S)</td>
<td>Low</td>
<td>Radanov et al. (1994b) (S)</td>
<td>Low</td>
<td>Inconclusive</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Sterling et al. (2006) (D)</td>
<td>Adequate</td>
<td>Inconclusive</td>
</tr>
<tr>
<td>Catastrophising</td>
<td>Nederhand et al. (2004) (D)</td>
<td>Adequate</td>
<td>Kivoja et al. (2005) (D)</td>
<td>Adequate</td>
<td>Inconclusive</td>
</tr>
<tr>
<td>Soderlund et al. (2000) (S)</td>
<td></td>
<td>Low</td>
<td>Kivoja et al. (2005) (S)</td>
<td>Adequate</td>
<td>Inconclusive</td>
</tr>
<tr>
<td>Coping strategies</td>
<td>Soderlund et al. (2000) (S)</td>
<td>Low</td>
<td>Kivoja et al. (2005) (S)</td>
<td>Adequate</td>
<td>Inconclusive</td>
</tr>
<tr>
<td>Somatisation</td>
<td>Hendriks et al. (2005) (D)</td>
<td>Adequate</td>
<td>Atherton et al. (2006) (S)</td>
<td>Adequate</td>
<td>Inconclusive</td>
</tr>
</tbody>
</table>

(S) Outcome measure based on symptomatic report. (D) Outcome measure based on disability or function.
greater post-traumatic stress (Sterling et al., 2005, 2006). Self-efficacy is a concept developed by Bandura (1977) and is defined as a personal belief of how successfully one can cope with difficult situations (Soderlund and Lindberg, 2002). Soderlund et al. (2000) and Kyhlback et al. (2002) used the Self-efficacy Scale (Altmair et al., 1993) which looks specifically at a patient’s confidence to perform activities of daily life despite pain. Post-traumatic stress refers to a stress reaction directly related to the traumatic event (i.e. the whiplash injury in this instance) measured using the Impact of Events Scale but it is not a true diagnosis of Post-traumatic Stress Disorder (PTSD) according to the criteria presented by the DSM-IV (American Psychiatric Association, 2000; Joseph, 2000).

No association was found between personality traits or general psychological distress and the development of LWS based on the results of 4 cohorts and 6 cohorts, respectively (moderate evidence). No association was found between wellbeing, social support, life control or psychosocial work factors based on the results of one cohort each (limited evidence). Findings regarding the following constructs were considered inconclusive: psychosocial stress not associated with the accident, previous psychological problems, blame and anger, perceived threat at the time of the accident, cognitive function, anxiety, depression, somatisation, irritability, familiarity with whiplash symptoms, fear avoidance beliefs, catastrophising, and coping strategies.

4. Discussion

This review highlights the need for further research as most findings were inconclusive or based on limited evidence. Self-efficacy and post-traumatic stress may be related to the development of LWS but these factors warrant further research.

4.1. Limitations

Meta-analysis was impossible due to the use of different outcome measures and prognostic factors. Also, the standard of reporting was poor and the data necessary for meta-analysis were frequently not reported. This meant the only quantitative analysis possible was a “vote counting” procedure where the number of studies with significant findings was compared to the number of studies with non-significant findings for each factor. This approach was also used by Scholten-Peeters et al. (2003) and is problematic because it does not consider effect size or strength of association. Meta-analysis of several studies with non-significant results may reveal an association that each study individually had too little power to detect. Studies that are underpowered may fail to reach statistical significance even when associations exist, so reliance on statistical significance may fail to find associations that would be revealed by meta-analysis. Meta-analysis would allow more definite conclusions as it would provide an estimate of the strength of association of each risk factor with LWS.

Publication bias is a problem for systematic reviews in general as studies with significant findings are more likely to be published. Particular to this review was the potential for bias due to the exclusion of non-English articles. However, of the 7 articles that were potentially eligible, 3 (Di Stefano and Radanov, 1993; Radanov et al., 1993c, 1994c) were also reported in English. Of the other 4 potentially eligible articles 2 had no abstract available in English (Kageyama et al., 1969; Foletti and Regli, 1987). The remaining two articles (Huber et al., 1993; Pujol et al., 2003) were both prospective studies with 62 and 122 subjects, respectively, but it was unclear from the abstracts whether they included any psychological factors. Attempts were made to contact both authors but these were unsuccessful.

4.2. Methodological issues

A major shortcoming of the included studies was that they failed to use outcomes with established test-retest reliability in pain populations. If an outcome measure is not reliable then results based on it are questionable. Outcome measures used in the research presented were extremely variable. For example, many studies used a dichotomous outcome where patients were categorised as recovered or non-recovered but these definitions varied. Mayou and Bryant (2002) defined non-recovered as the report of moderate or severe pain while Radanov et al. (1993a) defined it as the report of any symptoms. A lack of correlation has been demonstrated between pain and disability (Crombez et al., 1999) and for this reason a measure of both should be included in future research.

The appropriateness of measures used for the prognostic factors for this patient group also needs to be considered. The inconclusive findings for some constructs may be due to the tools used. For example, use of the Beck Depression Index in pain populations has been criticised because the items relating to somatic symptoms may reflect physical symptoms experienced by patients rather than their mood (Pines and Williams, 1999).

The reporting of statistical analysis of results was the most problematic in terms of methodological quality. Even when the investigator is primarily interested in one possible prognostic factor multivariate analysis is essential to control for bias (Szkl and Nieto, 2000; (p. 257)). Due to the multi-factorial nature of pain and disability many constructs may influence outcome. Some studies failed to carry out multivariate analysis but carried out high numbers of univariate analysis. Radanov et al. (1995) carried out over 90 univariate analyses. Under such circumstances associations will be found
due to type I errors. Univariate analysis is an essential step to select factors to be included in the multivariate analysis but conclusions based solely on univariate analysis are subject to bias and should be interpreted cautiously.

When assessing methodological quality points were awarded for carrying out multivariate analysis but often the analysis presented was uninformative and conclusions were still based on univariate analysis. Two articles did control for all 4 pre-specified factors considered necessary to reduce bias in this population demonstrating that this is achievable. Inadequate sample sizes were a frequent problem and larger studies are needed if comprehensive models are to be tested when considering prognostic factors in the development of LWS.

4.3. Future research

There were several factors for which the results did not show an association or were inconclusive even though they are thought to influence the transition from an acute to chronic state in conditions such as LBP. Psychological distress influences outcome following acute LBP (Pincus et al., 2002) and some initial analysis showed that distress influenced outcome following whiplash injury (Atherton et al., 2006). However, when injury severity was controlled for this was no longer true. A similar result was seen with fear-avoidance. Fear avoidance is a belief that certain activities should be avoided due to fear of causing pain or re-injury (Kori et al., 1990). Fear avoidance was related to outcome in univariate analysis (Nederhand et al., 2004) but not when considered in multivariate analysis along with injury severity (Sterling et al., 2005; Sterling et al., 2006). A similar effect was seen with catastrophising (Soderlund et al., 2000; Nederhand et al., 2004; Kivioja et al., 2005). This may suggest constructs such as distress, fear-avoidance and catastrophising are moderated by injury severity rather than being primary predictors of outcome. Further research is needed to understand the interaction between initial injury severity and these constructs as addressing these secondary factors may still be an important part of patient management.

The role of coping was also inconclusive. Coping has been shown to affect disability in acute LBP populations (Jones et al., 2006) and is closely related to self-efficacy. Research by Soderlund and Lindberg (2002) suggests that the coping styles adopted by patients influence the relationship between self-efficacy and disability. The role of coping in the development of LWS was investigated using pain as the outcome (Soderlund et al., 2000; Kivioja et al., 2005). Further research needs to use a measure of disability to assess if coping influences recovery in whiplash injuries as it appears to in LBP.

Scholten-Peeters et al. (2003) called for international consensus on a core set of relevant prognostic factors and the use of standardised outcome measures to facilitate this research but this has not happened. There is a need to continue to build on previous research with improved study design.

4.4. Previous systematic reviews

This review identified 16 articles that were not included in the earlier review by Scholten-Peeters et al. (2003). In light of this, differences between the two reviews would be expected. Results for self-efficacy and post-traumatic distress are reported in new research. The two reviews were in agreement that general psychological distress was not associated with the development of LWS. However, the presence of previous psychological problems was found to be associated with poor outcome by Scholten-Peeters et al. (2003), but was inconclusive in this review. Research pertaining to personality traits was deemed inconclusive by Scholten-Peeters et al. but we found moderate evidence that no association existed. Differences in the methodology used may also have contributed to the different findings. In this review outcome measures were based on the definition of LWS, meaning that studies with less than 6 months follow up or those using outcomes such as time to claim closure were excluded. Different criteria were also used to classify the quality of research. Scholten-Peeters et al. classified articles scoring 50% or more on the quality scoring as high quality research. We used three ratings of high, adequate and low quality. Scholten-Peeters et al. used an overall score to determine quality levels whereas this review considered the scores of each of the three sections of the quality assessment. This approach has made it more difficult for studies to achieve a high quality rating but it was felt that it reflected more accurately the quality of the research presented.

4.5. Clinical implications

Identifying prognostic factors has implications for patient management. Self-efficacy and other factors such as coping, catastrophising and fear-avoidance could be addressed through treatments such as physiotherapy. Physiotherapists are ideally placed to teach coping strategies, improve patients’ confidence in their ability to carry out activities and to influence how patients think about their symptoms. This approach is in line with the clinical guidelines recommended by Scholten-Peeters et al. (2002) but needs to be evaluated. Identifying prognostic factors may also assist in screening patients at risk of poor outcome allowing, for example, patients with high levels of post-traumatic stress to be referred for appropriate psychological management.
5. Conclusion

In recent years there has been an interest in the psychological aspects of whiplash injuries reflecting a better understanding of the multifaceted nature of pain and disability. However, this is an area that requires more rigorous research through well-designed sufficiently powered prognostic studies.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.pain.2007.04.035.

References

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Global Year Against Pain in Women
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Dysmenorrhea: Contemporary Perspectives

Classification/definition:
- Dysmenorrhea (painful periods) is traditionally classified as either primary dysmenorrhea – menstrual pain without pelvic pathology, with onset shortly after menarche, or secondary dysmenorrhea - pain associated with secondary pathology, and the onset may be years after menarche.
- Premenstrual syndrome (PMS) is defined as cyclical mood and behavioral changes occurring during 5 days prior to menses
- Premenstrual dysphoric disorder (PMDD) is the presence of severe affective symptoms during the luteal phase of the menstrual cycle, which may encompass depression, anxiety, concentration difficulties, appetite changes, and sleep changes that interfere with functioning in work, family, and social settings.

Epidemiology:
- Dysmenorrhea affects 40-90% of women.
- Primary dysmenorrhea is most common between the ages of 15-19 years, declining thereafter.
- 5-14% of women have regular school absenteeism as a result of symptoms.
- 13-51% of women have been absent at least once in their lives from school or work due to dysmenorrhea.
- Many cultures, such as some Mediterranean, Muslim, Hindu, and Chinese, still perceive menstruation as taboo and impure, resulting in reluctance of pain report and failure of healthcare delivery.

Associated risk factors:
- A low BMI is associated with increased risk of primary dysmenorrhea.
- A negative association has been described between consumption of fruit, eggs, and fish and primary dysmenorrhea, perhaps related to intake of omega-3 fatty acids, calcium, and magnesium.
- Psychosocial determinants are also important, as poor mental health, somatiform symptoms, decreased coping ability, depression, and anxiety have been found to be strong determinants of dysmenorrhea.
- Primary dysmenorrhea often co-occurs with nausea and vomiting, diarrhea, tiredness, and feelings of irritability.
  - Many idiopathic pain disorders (IBS, IC/PBS, vulvodynia, dyspareunia, temporomandibular disorder, and migraines) are frequently co-morbid with primary dysmenorrhea.
- Secondary dysmenorrhea presents in association with endometriosis, presence of an IUD, pelvic inflammatory disease, adenomyosis, uterine myomas and adhesions, or cervical obstruction from mullerian anomalies.
- Smoking has been associated with an increased risk of dysmenorrhea, but alcohol is not consistently linked to dysmenorrhea risk.

Presentation:
- Primary dysmenorrhea pain precedes the onset of a menstrual period and typically lasts 2-3 days.
- Secondary dysmenorrhea pain may start 1-2 weeks before menstrual flow and persist beyond the cessation of bleeding.
- The classic labor-like, suprapubic, colicky pain of dysmenorrhea may radiate to the lumbosacral region or anterior thigh.
- Associated visceral symptoms include nausea, vomiting, or diarrhea.
- On examination, prominent uterine tenderness is found during menstruation, which may also extend outside of menses in secondary dysmenorrhea.

Pathophysiology:
- The exact etiology is unclear, but may reflect upregulated cyclooxygenase (COX) enzyme activity and prostanoid synthase activity, which are normally activated in the late luteal phase through release of progesterone inhibition of arachidonic acid production.
- Endometrial prostaglandin production results in increased uterine contractions and relative myometrial ischemia.
- Abnormal uterine contraction patterns and alterations in uterine blood flow are also noted in some dysmenorrhea sufferers.
• Somatization and poor coping are also positively associated with menstrual pain intensity, suggesting that central factors should also be considered.

Treatments:
• Conservative measures such as non-steroidal anti-inflammatories (NSAIDs) are used as first-line therapy, ideally initiated prior to the onset of menses by 48 hours to decrease COX substrate.
  o A usual trial of 3-6 months of therapy is conducted before additional evaluation for causes of secondary dysmenorrhea.
• Vitamin and mineral supplementation (i.e. fish oil, thiamine, magnesium, or pyridoxine) may also be effective based on small studies.
• Local nerve stimulation (TENS, hot compresses, acupuncture) has also been shown to be effective in small studies.
• If NSAIDs fail, combined oral contraceptives are often employed to inhibit ovulation and suppress endometrial growth. By maintaining an endocrine state of the early proliferative phase, this approach also decreases prostaglandin levels.
• Continuous progestins (oral, intramuscular or via intrauterine device) may be needed to induce anovulation in recalcitrant cases.
  o While androgen derivatives (danocrine) also induce anovulation, their severe virilizing side effects make them less attractive.
• In more severe cases, short-courses of opioids should be considered for managing breakthrough pain.
• Exirpative surgery (laparoscopic excision of endometriotic lesions, or leiomyoma) should be reserved only if the above fail, while nerve destructive procedures should be used only cautiously.
  o While randomized controlled trials demonstrate that presacral neurectomy is an effective treatment for dysmenorrhea, this procedure does have a risk for causing permanent visceral side effects.

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