

A literature review reveals that trials evaluating treatment of non-specific low back pain use inconsistent criteria to identify serious pathologies and nerve root involvement

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Objectives: The broad aim of this study was to assess the homogeneity of patients included in trials of non-specific low back pain (NSLBP). To do this, we investigated the consistency and clarity of criteria used to identify and exclude participants with serious pathologies and nerve root compromise in randomized controlled trials, investigating interventions for NSLBP.

Methods: We searched Medline database for randomized controlled trials of low back pain (LBP) published between 2000 and 2009. We then randomly selected and screened trials for inclusion until we had 50 eligible trials. Data were extracted on the criteria used to identify cases of serious conditions (e.g. cancer, fracture) and nerve root involvement.

Results: The majority of papers (35/50) explicitly excluded patients with serious pathology. However, the terminology used and examples given were highly variable. Nerve root involvement was an exclusion criterion in the majority but not all studies. The criteria used for excluding patients with nerve root involvement varied greatly between studies. The most common criteria were 'motor, sensory or reflex changes' (nine studies), followed by 'pain radiating below the knee' (five studies) and 'reduced straight leg raise which reproduces leg pain' (five studies). In half of the included studies, the criteria used, while alluding to nerve root involvement, were not explained adequately for us to determine the types of patients included or excluded.

Discussion: The inconsistent and unclear criteria used to identify cases of serious pathology and nerve root compromise means that published trials of LBP likely include heterogeneous patient populations. This trait limits our ability to make comparisons across trials or pool studies. Standardization and consensus is important for future research.

Keywords: Low back pain, Sciatica, Nerve root compromise, Red flags

Introduction

Low back pain (LBP) guidelines recommend the application of a diagnostic triage in (LBP) management, to differentiate patients with non-specific low back pain (NSLBP) from those with serious pathologies such as fracture and cancer or nerve root involvement.^{1,2} However, many guidelines do not provide clear or consistent criteria for identifying the patients with serious pathologies or nerve root involvement. The terms used to describe patients

with nerve root involvement vary and include radicular syndrome,³ sciatica,⁴ nerve root compression,⁵ nerve root compromise,⁶ and radiculopathy.⁷ These terms are generally poorly defined with inconsistent diagnostic criteria between authors. A recent study⁸ of (LBP) guidelines identified that different guidelines reported different criteria for identifying patients with nerve root involvement.

Clear consistent criteria for identifying those with serious pathology or nerve root involvement are important for future research and interpretation of previous research studies. The types of patients included in trials of (NSLBP) will be determined

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largely by the criteria used to exclude patients with serious pathology and nerve root involvement. Estimates of the proportion of patients with nerve root involvement vary, but can be as high as 25%.⁹ Therefore, the criteria for excluding these patients are particularly important, as they are likely to significantly impact on the types of patients included in trials of NSLBP. If studies of NSLBP include different types of patients, then it may limit the ability to pool findings from randomized trials or prognostic studies. For example, patients with nerve root involvement are likely to have different prognoses, and responses to treatment, to those with NSLBP, so it is particularly important to standardize exclusion criteria used to identify those with nerve root involvement.

At present, it is not clear whether studies have used a consistent approach to identify and exclude participants with serious pathologies or nerve root involvement in clinical studies of NSLBP. Therefore, this study investigated the consistency and clarity of criteria used to exclude patients with serious pathologies and nerve root involvement in a random sample of randomized controlled trials (RCTs), investigating interventions for NSLBP. A secondary aim was to describe the range of criteria used to characterize nerve root compromise in trials of NSLBP.

Materials and Methods

Search strategy

We identified a random sample of 50 RCTs published between 2000 and 2009 that evaluated treatment for NSLBP via a search of Medline. The search strategy used keywords describing LBP (low back pain OR low back ache OR sciatica OR lumbago) AND randomized controlled trials (randomized controlled trial OR controlled clinical trial OR Randomized Controlled Trials OR Random Allocation OR Double-Blind Method OR Single-Blind Method OR Animal/not human OR clinical trial OR clinic\$ adj25 trial\$ OR ((single\$ or double\$ or treble\$ or triple\$) adj (mask\$ or blind\$)) OR random\$ OR Cross-Over Studies NOT animal NOT review NOT guidelines). All identified trials were transferred to a reference managing program and allocated a random number generated in Excel. Potential studies were then screened for inclusion starting with the study allocated random number 1. We then continued screening studies in the order of their random number allocation until 50 trials were identified that met the inclusion criteria. Screening was performed by title and abstract and then by full text. All stages of screening were performed by two authors with discrepancies resolved by discussion. These 50 trials formed the data for this study (Fig. 1).

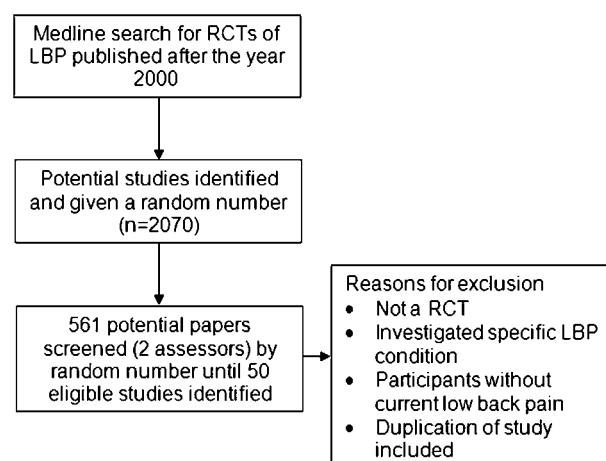


Figure 1 Flow chart: study selection.

Inclusion criteria

Studies were included if they met all of the following criteria:

- a RCT;
- study population of patients with NSLBP;
- investigated an intervention for NSLBP;
- published in English or Portuguese.

Data extraction

Data were extracted on the exclusion criteria reported by each trial. These data indirectly described the patients included with NSLBP. Authors reviewed the exclusion criteria of each trial, to ascertain if participants were excluded based on the presence of serious pathologies and/or nerve root involvement and the criteria used. Each trial was assessed against a number of pre-planned criteria for excluding patients with nerve root involvement. The criteria were motor/sensory/reflex changes, unilateral leg pain more intense than back pain, pain radiates below the knee and reduced straight leg raise. Authors determined if criteria used to exclude patients with serious pathologies and nerve root involvement were: (1) clearly stated as exclusion criteria, (2) not stated as exclusion criteria, or (3) if it was ambiguous or unclear.

To further summarize the types of patients included in each of the trials we rated each trial from 1 to 5 based on criteria used for inclusion/exclusion of patients with nerve root involvement. The definitions of each category are described in Table 1.

Results

The search identified a total of 2070 potential papers. We screened 561 papers to find 50 that met the inclusion criteria. Papers were excluded on the basis of their design (not RCTs), their target population (not NSLBP) and/or because they failed to investigate a treatment for NSLBP. Included trials investigated a range of interventions including acupuncture, physiotherapy, exercise, manual therapy, massage, and advice.

The majority of papers (35/50, 70%) explicitly excluded patients with serious pathologies. However, the terminology used and examples given were highly variable. For example, terms used included, ‘major trauma or systemic disease’,¹⁰ ‘potentially serious pathology’,¹¹ ‘non-mechanical origin’,¹² and ‘red flags’.¹³ Ambiguous phrases which may or may not have been referring to serious pathologies were used in a further nine (18%) papers (see Table 2). Several

of the studies we rated as ambiguous, referred to ‘specific’^{14–19} or exact diagnoses of LBP (Table 2). Six studies (12%) did not report any exclusion criteria for identifying patients with potential serious pathology.

While most studies (38/50, 76%) alluded to excluding people with nerve root involvement, the criteria used varied greatly between studies and no single criterion was used by more than nine studies (Fig. 2). The most common criterion was ‘motor, sensory or

Table 1 Description of included patients (nerve root involvement)

Description of included patients	Studies
1. LBP above buttock crease only (explicitly excludes any referred pain below buttocks or neurological signs or symptoms)	Itoh <i>et al.</i> ¹⁰ Dreiser <i>et al.</i> ²²
2. LBP ± somatic type leg pain (excludes pain due to nerve root irritation, i.e. radicular pain, positive straight leg raise, with or without exclusion of those with motor, sensory or reflex changes)	Toda <i>et al.</i> ²³ Ahlqwist <i>et al.</i> ²⁴ Childs <i>et al.</i> ²⁶ Katz <i>et al.</i> ²⁷ Brinkhaus <i>et al.</i> ²⁵
3. LBP and any leg pain but excluded those with motor, sensory or reflex changes	Hurwitz <i>et al.</i> ²⁸ Eisenburg <i>et al.</i> ²⁹ Hurley <i>et al.</i> ³⁰ Haas <i>et al.</i> ³¹ Teyhen <i>et al.</i> ³² Brennan <i>et al.</i> ³³
4. LBP and any leg pain or motor, sensory or reflex changes	Hay <i>et al.</i> ¹¹ Roberts <i>et al.</i> ¹³ Penttinen <i>et al.</i> ¹⁸ Heymans <i>et al.</i> ³⁴ Kendrick <i>et al.</i> ³⁵ Yip <i>et al.</i> ³⁶ Frerick <i>et al.</i> ³⁷ Lee <i>et al.</i> ³⁸ Grunnesjo <i>et al.</i> ³⁹ Marshall <i>et al.</i> ⁴⁰ Gabis <i>et al.</i> ⁴¹ Chiradejnant <i>et al.</i> ⁴²
5. Unable to classify due to inadequate information	Tuzun <i>et al.</i> ¹² Kaapa <i>et al.</i> ¹⁴ Hernandez <i>et al.</i> ¹⁵ Yakhno <i>et al.</i> ¹⁶ Helmhout <i>et al.</i> ¹⁷ Helmhout <i>et al.</i> ¹⁹ Smeets <i>et al.</i> ²⁰ Inoue <i>et al.</i> ²¹ Yelland <i>et al.</i> ⁴⁹ Yip <i>et al.</i> ⁵⁰ Chrubasik <i>et al.</i> ⁵¹ Steenstra <i>et al.</i> ⁵² Rasmussen <i>et al.</i> ⁵³ Preyde <i>et al.</i> ⁵⁴ Seferlis <i>et al.</i> ⁵⁵ Storheim <i>et al.</i> ⁵⁶ Lierz <i>et al.</i> ⁵⁷ Bergoldt <i>et al.</i> ⁵⁸ Hawk <i>et al.</i> ⁵⁹ Molde Hagen <i>et al.</i> ⁶⁰ Chrubasik <i>et al.</i> ⁶¹ Goldby <i>et al.</i> ⁶² Snook <i>et al.</i> ⁶³ Prady <i>et al.</i> ⁶⁴ Leibing <i>et al.</i> ⁶⁵

Nerve Root Involvement Exclusion Criteria

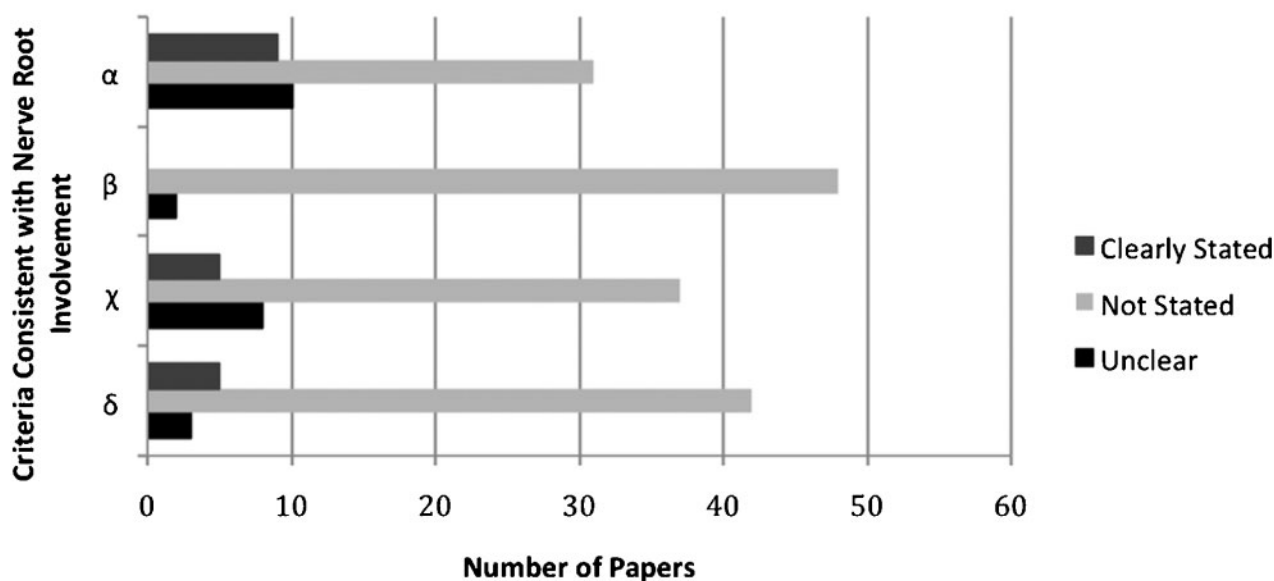


Figure 2 Criteria for exclusion of nerve root involvement ($n=50$). α , motor, sensory, reflex changes; β , leg pain greater than back pain; χ , pain radiates below the knee; δ , reduced straight leg raise which reproduces pain.

reflex changes' (nine studies), followed by 'pain radiating below the knee' (five studies) and 'reduced straight leg raise which reproduces leg pain' (five studies) (Fig. 2). In half of the included studies, the criteria used, while alluding to nerve root involvement, were not explained adequately for us to determine the types of patients included or excluded (Table 1, category 5). Examples of terms used that we considered ambiguous were sciatic nerve involvement,¹⁵ current nerve root pathology,²⁰ other relevant neurologic diseases,¹⁹ and leg symptoms.²¹ Table 1 presents the types of patients included in each study, based on the reported

exclusion criteria for nerve root involvement. The studies we could confidently classify included patients with quite different presentations of nerve root involvement. Some studies used very strict criteria where only patients with LBP and no pain extending past the knee were included.^{10,22} Other studies included patients with leg pain but excluded them, if they had signs of nerve root irritation (i.e. radicular pain, positive straight leg raise, with or without exclusion of those with motor, sensory or reflex changes).²³⁻²⁷ Some studies only excluded patients when motor, reflex or sensory deficits were present.²⁸⁻³³ Other studies did not appear to

Table 2 Unclear criteria for exclusion of serious pathologies

'Unclear' serious pathology exclusion criteria	Study
All patients were examined by an orthopaedic surgeon prior to enrolment, and any whose symptoms or findings on imaging indicated the need for medication or surgery or suggested an underlying disease were excluded	Inoue <i>et al.</i> ²¹
Specific back disorder	Kaapa <i>et al.</i> ¹⁴
Back pain due to fractured vertebrae, herniated or degenerated disks	Hernandez-Reif <i>et al.</i> ¹⁵
Other serious illness, which could influence on their sleep	Bergholdt <i>et al.</i> ⁵⁸
Specific spinal pathology or symptoms related to other pathologies	Yakhno <i>et al.</i> ¹⁶
Specific LBP, defined as herniated disc, ankylosing spondylitis, spondylolisthesis or other relevant	Helmhout <i>et al.</i> ¹⁷
(Back pain non-specific), those with exact diagnoses being excluded	Penttinen <i>et al.</i> ¹⁸
Presence of severe postural abnormality or neuromuscular disorder, previous diagnosis of pathology (confirmed by magnetic resonance imaging or radiograph) which would contraindicate exercise or manipulation	Marshall <i>et al.</i> ⁴⁰
Specific LBP, defined as herniated disk, ankylosing spondylitis, spondylolisthesis, or other relevant neurologic diseases	Helmhout <i>et al.</i> ¹⁹

exclude even those patients with motor, reflex or sensory deficits.^{11,13,18,34-42}

Discussion

Our review of the literature indicated that the criteria used to identify patients with serious disease and nerve root involvement were not consistent across RCTs. Many of the papers adopted ambiguous or vague exclusion criteria and therefore, failed to clearly outline to the reader what type of patient was included in the trial. Interestingly, there was no consistency between trials regarding the degree of nerve root involvement that warrants exclusion from a trial of NSLBP. This is an important finding as it strongly suggests that trials reported to include patients with NSLBP likely include heterogeneous patients.

In a recent review of 11 different national clinical guidelines for NSLBP, Koes and colleagues¹ found that although all of the guidelines recommended the use of a diagnostic triage, a number of them only distinguished NSLBP from LBP caused by a serious pathology. The authors commented that patients with nerve root involvement were variously included in the serious pathology or NSLBP group for management. The findings of Koes *et al.*¹ align with the results of our review, as we found that although the majority of trials excluded those with serious pathologies, they differed markedly in terms of the degree of neurological impairment that would constitute evidence of nerve root involvement.

Although 70% of the trials in this review explicitly excluded LBP caused by serious pathologies, there was little consistency in the terminology or examples used to do so. With such variability, it is unclear if different trials are excluding the same types of patients. One area of confusion identified is the common reference to terms such as 'specific back disorder' or an 'exact diagnosis'. In many cases, it is unclear if authors used these terms to exclude patients with a specific but non-serious spinal pathology (e.g. disc protrusion, disc degeneration, spondylolisthesis) or were they excluding patients with a specific and serious spinal pathology (e.g. metastatic cancer of the spine or a vertebral fracture). Currently, it is unclear where specific spinal pathologies like canal stenosis, spondylolisthesis or disc herniation fit in the diagnostic triage. Until future expert consensus on this issue is reached, we suggest authors avoid terms like specific disorders and clearly explain the condition excluded from a trial.

Haswell *et al.*⁸ found that LBP clinical guidelines differed considerably in the criteria they used to diagnose 'nerve root syndrome'. A number of these guidelines outlined clinical assessment findings like nerve conduction block signs,⁴³⁻⁴⁷ a reduced straight leg raise that reproduces pain,^{44,45,47} unilateral leg

pain worse than back pain,^{44,45,47} as consistent with nerve root syndrome. Our review found the lack of consistency in defining nerve root involvement in guidelines was also present in published trials of NSLBP.

While most studies in our review alluded to excluding patients with nerve root involvement the criteria used varied greatly between studies (Table 1). The result of this is that the patients included in these trials of NSLBP range from those with no pain extending past the buttock to those with neurological signs of motor sensory or reflex changes. Therefore, these papers have potentially included patients with quite different prognoses and responses to the intervention applied. Previous studies show that compared to people with only back pain people with 'sciatica' have more persistent and severe pain, greater disability and consume more healthcare resources.^{9,48} This has important implications for the external validity of different trials and also for systematic reviews which typically pool the results from these studies.

Our results highlight an important issue in NSLBP research, how do we ensure homogeneous study populations between trials? When we consider NSLBP research, the study population of interest is achieved by excluding other causes of LBP, i.e. serious pathologies and/or neurological involvement. Therefore, in order to achieve homogeneous study populations between trials, there is a need for homogenous exclusion criteria for the other causes of low back pain. Consensus expert definition of nerve root involvement and what constitutes serious pathology would be very important in the field.

Limitations

A limitation of this study is that we did not include all trials of NSLBP and instead included a random sample of trials. However, we believe we have gained a representative sample that highlights the inconsistent and unclear nature of the exclusion criteria used in trials of NSLBP. It is possible that some publication bias was introduced as we only conducted a literature search in Medline, and a language bias may have been introduced as we only looked at papers published in English and Portuguese. However, we believe inclusion of studies published in different databases or in different languages would be unlikely to change the key findings. Our study focused on potential differences in patients included in trials of NSLBP due to the exclusion criteria for serious pathologies and nerve root involvement. There are many other important reasons why patients in trials of NSLBP may be heterogeneous between studies. Examples include chronicity of patients, the setting (e.g. primary or secondary care) and the age of participants. While these are clearly important, they were not the focus of the current study.

Conclusion

The current study highlights that the criteria used to exclude patients with serious pathologies and neurological conditions are often not reported or ambiguous. Even when reported the criteria especially for nerve root involvement varies greatly across published trials. There is a clear need for consensus on what constitutes serious pathology and nerve root involvement in patients with LBP.

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