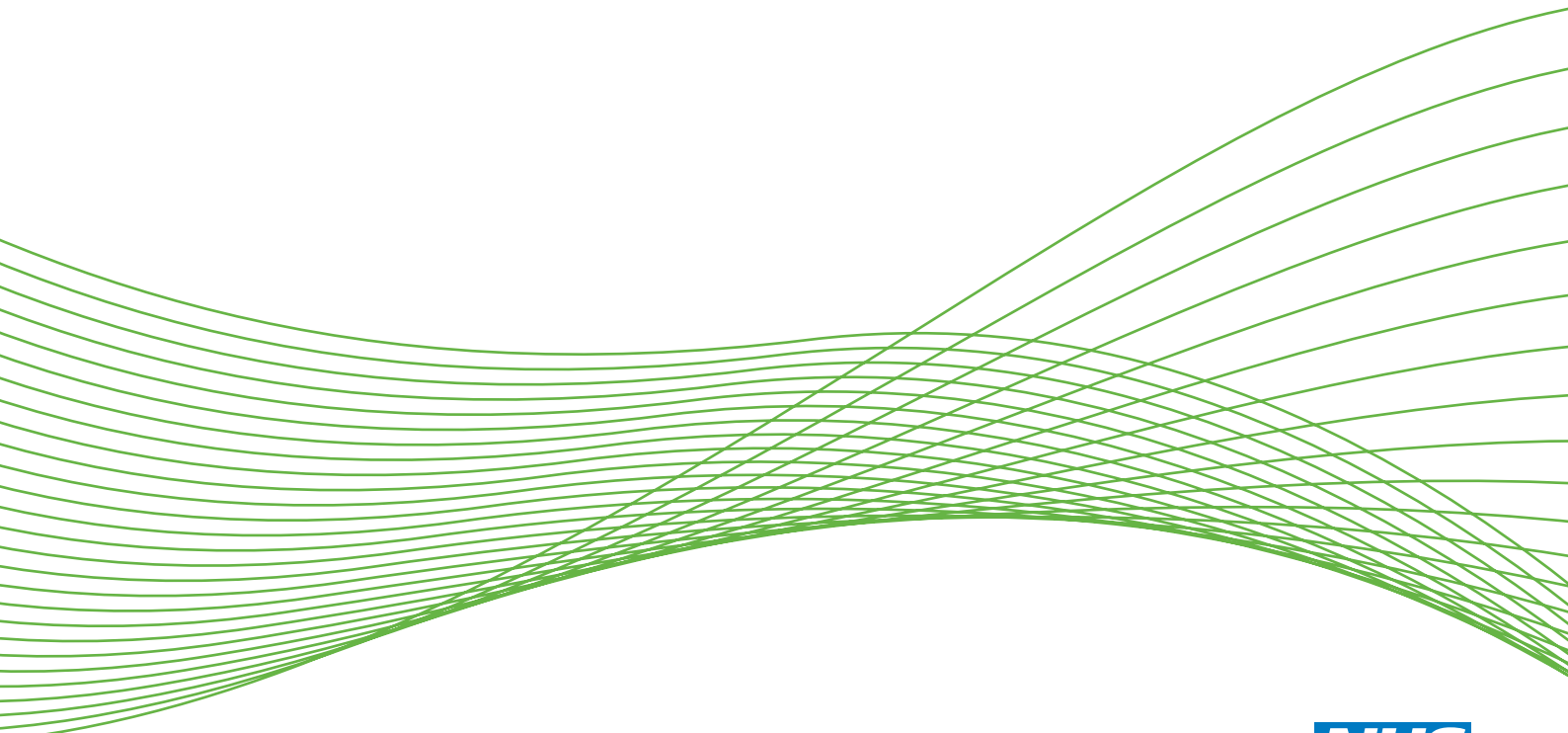# The diagnostic utility and cost-effectiveness of selective nerve root blocks in patients considered for lumbar decompression surgery: a systematic review and economic model

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NHS

National Institute for Health Research

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This report

Abstract

The diagnostic utility and cost-effectiveness of selective nerve root blocks in patients considered for lumbar decompression surgery: a systematic review and economic model

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Background: Diagnostic selective nerve root block (SNRB) involves injection of local anaesthetic, sometimes in conjunction with corticosteroids, around spinal nerves. It is used to identify symptomatic nerve roots in patients with probable radicular pain that is not fully concordant with imaging findings.

Objectives: (1) Determine the diagnostic accuracy of SNRB in patients with low back and radiating pain in a lower limb; (2) evaluate whether or not accuracy varies by patient subgroups; (3) review injection-related adverse events; and (4) evaluate the cost-effectiveness of SNRB.

Data sources: MEDLINE, EMBASE, Science Citation Index, Bioscience Information Service (BIOSIS), Latin American and Caribbean Health Sciences Literature (LILACS) and grey literature databases were searched from inception to August 2011. Reference lists of included studies were screened.

Methods: A systematic review (SR) of studies that assessed the accuracy of SNRB or adverse events in patients with low back pain and symptoms in a lower limb for the diagnosis of lumbar radiculopathy. Study quality was assessed using the quality assessment of diagnostic accuracy studies (QUADAS)-2 checklist. We used random-effects meta-analysis to pool diagnostic accuracy data. Decision tree and Markov models were developed, combining SR results with information on the costs and outcomes of surgical and non-surgical care. Uncertainty was assessed using probabilistic and deterministic sensitivity analyses.

Results: Five studies assessed diagnostic accuracy: three diagnostic cohort and two within-patient case–control studies. All were judged to be at high risk of bias and had high concerns regarding applicability. In individual studies, sensitivity ranged from 57% [95% confidence interval (CI) 43% to 70%] to 100% (95% CI 76% to 100%) and specificity from 9.5% (95% CI 1% to 30%) to 86% (95% CI 76% to 93%). The most reliable estimate was judged to come from two cohort studies that used post-surgery outcome as the reference standard; summary sensitivity and specificity were 93% (95% CI 86% to 97%) and 26% (95% CI 5% to 68%), respectively. No study provided sufficient detail to judge whether or not accuracy varied by patient subgroup. Seven studies assessed adverse events. There were no major or permanent complications; minor complications were reported in 0–6% of patients. The addition of SNRB to the

diagnostic work-up was not cost-effective with an incremental cost per quality-adjusted life-year of £1,576,007. Sensitivity analyses confirmed that SNRB was unlikely to be a cost-effective method for diagnosis and planning surgical therapy.

Limitations: We identified very few studies; all were at high risk of bias. The conduct and interpretation of SNRBs varied and there was no gold standard for diagnosis. Limited information about the impact of SNRB on subsequent care and the long-term costs and benefits of surgery increased uncertainty about cost-effectiveness.

Conclusions: There were few studies that estimated the diagnostic accuracy of SNRB in patients with radiculopathy and all were limited by the difficulty of making a reference standard diagnosis. Summary estimates suggest that specificity is low, but results are based on a small number of studies at a high risk of bias. Based on current weak evidence, it is unlikely that SNRB is a cost-effective method for identifying the symptomatic nerve root prior to lumbar spine surgery. Future research should focus on randomised controlled trials to evaluate whether or not SNRB improves patient outcomes at acceptable cost.

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Contents

Glossary

Clinical terms

Decompression surgery A surgical procedure designed to relieve pressure on a lumbar nerve root usually undertaken within the lumbar spinal canal. The procedure involves surgical removal of bone, ligament and or disc material which is compressing one or more nerve roots.

Lumbar disc herniation Prolapse of disc material into the spinal canal, lateral recess or neural foramen.

Lumbar radiculopathy Dysfunction of one or more nerve roots in the lumbar spine, characterised by pain and sensory and motor disturbances and often caused by compression of a nerve root(s).

Lumbar spine Vertebrae between the thoracic and sacral vertebrae designated L1–L5.

Radicular pain Pain which radiates along a nerve and is perceived to be in the distribution of that nerve.

Sciatica A lay term for radicular pain which radiates from the lower back to the buttocks, back of the thigh, and calf and foot, often associated with sensory disturbance in the same distribution.

Selective nerve root block Injection of local anaesthetic with or without other substances such as a steroid around spinal nerve root.

Spinal stenosis Narrowing of the spinal canal and/or lateral recesses resulting in compression of the cauda equina or individual nerve roots in the lateral recesses.

Zygapophyseal joint The paired synovial joints which lie posterolateral to the canal and together with the disc constitute a spinal motion segment.

Diagnostic accuracy terms

Diagnostic case–control study Diagnostic accuracy study in which the index test results of a series of patients with an established diagnosis are compared with the index test results of a non-diseased control group.

Within-patient case–control study Study in which each patient acts as his or her own control. For example, the nerve root block is performed on a nerve root clinically and radiologically confirmed to be the source of radiculopathy. A second block is performed in the same patient at a different site known not to be the source of radicular symptoms.

Diagnostic cohort study Diagnostic accuracy study in which a group of individuals with suspected disease undergo both the index test and the reference standard, and the results of the two tests are compared.

False-negative A test result which indicates that a person does not have the disease when that person actually does have the disease.

False-positive A test result which indicates that a person does have the disease when that person actually does not have the disease.

Index test New diagnostic test under examination.

Receiver operating characteristic curve A receiver operating characteristic curve represents the relationship between the 'true-positive fraction' (sensitivity) and the 'false-positive fraction' (specificity). It displays the trade-offs between sensitivity and specificity as a result of varying the cut-off value for positivity in case of a continuous test result.

Reference standard Established test(s) against which the accuracy of a new test for detecting a particular condition can be evaluated.

Sensitivity (true-positive rate) The proportion of individuals with the target condition who are correctly identified by the index test.

Specificity (true-negative rate) The proportion of individuals free of the target condition who are correctly identified by the index test.

True-negative A person without the disease correctly identified as negative by the index test.

True-positive A person with the disease correctly identified as positive by the index test.

Economic evaluation terms

Cost-effectiveness acceptability curve A way of illustrating cost-effectiveness results by graphing the probability that the intervention is cost-effective (*y*-axis) against the maximum that society is willing to pay for an improvement in health (*x*-axis).

Cost-effectiveness plane A way of illustrating cost-effectiveness results by graphing the mean incremental cost and effectiveness on a four-quadrant graph. Interventions that are more costly and more effective fall in the north-east quadrant.

Incremental cost-effectiveness ratio The difference in costs between one intervention and an alternative, divided by the difference in outcomes.

Quality-adjusted life-year A measure of benefit of health care combining the impact of both expected length of life and quality of life.

List of abbreviations

CEAC	cost-effectiveness acceptability curve	PEVPI	partial expected value of perfect information
CI	confidence interval	PSA	probabilistic sensitivity analysis
CT	computed tomography	PSS	personal social services
EQ-5D	European Quality of Life-5 Dimensions	QALY	quality-adjusted life-year
FN	false-negative	QUADAS	quality assessment of diagnostic accuracy studies
FP	false-positive	RCT	randomised controlled trial
HRG	Healthcare Resource Group	SNRB	selective nerve root block
ICER	incremental cost-effectiveness ratio	SPORT	Spine Patient Outcomes Research Trial
LDH	lumbar disc herniation	SR	systematic review
LR	lumbar radiculopathy	TN	true-negative
MRI	magnetic resonance imaging	TP	true-positive
NICE	National Institute for Health and Care Excellence	VAS	visual analogue scale

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices, in which case the abbreviation is defined in the figure legend or in the notes at the end of the table.

Executive summary

Background

During the course of a year, 36–48% of British adults recall having low back pain, with 58–62% of adults experiencing low back pain at some point in their lives. In the UK, the economic burden of back pain in terms of health-care costs and lost productivity is around £12B. In most cases, the pain will resolve after a few days or weeks, but in some patients pain may not resolve and becomes chronic. Patients with chronic pain often develop significant disability and have impaired quality of life. Patients may develop referred symptoms including pain, sensory disturbance (e.g. numbness) and weakness extending to the leg. In some patients, lower limb symptoms are caused by inflammation or compression of a spinal nerve root and this is termed lumbar radiculopathy (LR).

The exact cause of low back and leg pain may be difficult to diagnose. The distinction between radiculopathy and other types of referred lumbar spine pain is crucial for treatment planning. In carefully selected patients, decompressive lumbar surgery (e.g. discectomy) is more effective than conservative care in rapidly relieving leg pain and reducing disability. In most patients, the diagnosis of radiculopathy is made by careful correlation of clinical signs and symptoms (e.g. pain distribution, paresis, straight-leg raising test) and imaging findings (e.g. evidence of disc herniation and nerve root compression) from magnetic resonance imaging or computed tomography scans. Neither clinical findings nor anatomical imaging have perfect diagnostic accuracy and, not infrequently, the clinical and imaging findings are discordant. In patients with suspected LR in whom the clinical and imaging findings are equivocal or discordant, diagnostic uncertainty remains. Before embarking on invasive therapy (e.g. surgery) to decompress the lumbar nerve root, additional diagnostic tests such as selective nerve root blocks (SNRBs) are used to help clinicians decide between surgical and conservative care.

Objectives

This project aimed to:

1. Conduct a systematic review (SR) to determine the diagnostic performance of SNRB in patients with probable radicular pain that is not fully concordant with the imaging findings prior to lumbar decompression surgery.
2. Evaluate whether or not the diagnostic accuracy of SNRB varies by patient subgroup (e.g. patients with suspected radiculopathy at more than one level of the lumbar spine).
3. Conduct a SR to summarise the evidence on the incidence of procedure-related complications of diagnostic SNRB.
4. Conduct a SR of previous economic studies of the use of SNRB in patients with suspected LR and develop a cost-effectiveness model to evaluate the cost-effectiveness of using SNRB in patients with discordant clinical and imaging findings, including value of information analysis.

Methods

We developed and followed a protocol for all stages of the review. Studies were identified through searches of electronic databases, internet searches and scanning reference lists of included papers. Published and unpublished studies in any language were eligible for inclusion. Two reviewers screened titles and abstracts for relevance. Full papers of potentially relevant studies were obtained and assessed for inclusion by one reviewer and checked by a second. To be eligible for the diagnostic accuracy review,

studies had to report on patients with low back pain and symptoms in a lower limb, and the diagnostic accuracy of SNRB administered under radiological guidance had to be assessed against a reference standard for the diagnosis of LR: studies had to report sufficient data to allow extraction of a 2 × 2 table of test performance. To be eligible for the review of adverse events, studies had to report the administration of a diagnostic SNRB in patients with LR. Data extraction was performed by one reviewer and checked by a second. Four reviewers independently assessed the quality of diagnostic accuracy studies using the quality assessment of diagnostic accuracy studies (QUADAS)-2 checklist and discrepancies were resolved through discussion. The methodological quality of studies reporting on adverse events was not formally assessed. Data were extracted to populate 2 × 2 tables of test performance and were used to calculate sensitivity, specificity and 95% confidence intervals (CIs). Study estimates of sensitivity and specificity were plotted in summary receiver operating characteristic space. Random-effects meta-analysis was used to calculate summary sensitivity and specificity separately for diagnostic cohort studies that used intraoperative findings and those that used post-surgical follow-up as a reference standard. Owing to the substantial differences between the control injections used in the within-patient case–control studies, we did not pool data from these studies. Data from studies on adverse events were combined in a narrative summary.

Based on data on diagnostic accuracy from the SR, we developed a decision tree and Markov model to estimate the incremental costs and effects of adding SNRB to the diagnostic work-up of suspected LR. The effectiveness and post-treatment costs of surgery and conservative care were taken from randomised controlled trial (RCT) evidence. Evidence about additional parameters of the model was identified from the medical literature and routine data sources. We developed two models to estimate the incremental cost per quality-adjusted life-year (QALY) in patients with suspected single- and two-level nerve root compression.

Results of the diagnostic accuracy systematic review

The searches identified 11,211 titles and abstracts; of these, 138 were considered potentially relevant, retrieved and screened as full papers. Five studies ($n = 241$ patients; range 15–83 per study) were included in the review: two within-patient case–control studies, one prospective diagnostic cohort study and two retrospective diagnostic cohort studies. In all patients in the case–control studies, the source of the radiculopathy was confirmed by concordant clinical and radiological or surgical findings prior to the use of SNRB. These concordant findings formed the reference standard against which the results of injections at the symptomatic nerve root and adjacent asymptomatic sites were compared. The diagnostic cohort studies recruited patients with suspected LR but equivocal or discordant clinical and radiological findings. These studies used intraoperative findings and/or outcome following surgery as the reference standard.

There was substantial variation in the results of the studies: sensitivity ranged from 57% to 100% and specificity from 10% to 86%. All studies were judged to be at a high risk of bias. Both within-patient case–control studies selected patients with concordant clinical and imaging findings and, therefore, their findings were judged to have poor applicability to patients with discordant clinical and imaging findings. All three cohort studies were judged to be at a high risk of bias, as the decision to perform surgery (the reference standard) was not independent of the SNRB result. The reference standard was judged to be at a high risk of bias in all five studies, as there was no gold standard for the diagnosis of radiculopathy.

Based on the two cohort studies that used an intraoperative reference standard the sensitivity was 93.5% (95% CI 84.0% to 97.6%) and specificity was 50.0% (95% CI 16.8% to 83.2%). Summary sensitivity was similar in the two studies that used post surgery as the reference standard at 93.3% (95% CI 85.8% to 97.0%), but specificity was lower at 25.6% (95% CI 5.4% to 67.5%). Owing to the differences in patient selection, type of control injection and reference standards between within-patient case–control studies and the diagnostic cohort studies we decided that it would be inappropriate to statistically combine the results of these studies.

Results of the selective nerve root block-related adverse events systematic review

Seven studies reported on SNRB-related adverse events. Only one study reported on the complications of SNRBs as the primary outcome of interest. This study found that minor and transient complications were encountered in 98 of the 1777 total patient visits (during which 2217 injections were delivered to 1203 patients), giving an overall per-patient visit complication rate of 5.5%. One other study reported that complications were encountered in four patients (3.8%) who experienced aggravated pain for 1–2 days following SNRB. The remaining five studies (range $n = 15$–117) reported that there were no complications. None of the studies reported major or permanent complications resulting from SNRB.

Results of the economic evaluation

Our economic model estimated that, for patients with suspected single-level nerve root compression, the addition of SNRB to the diagnostic work-up was not cost-effective, with an incremental cost per QALY gained of £1,576,000, which is greater than conventional thresholds for acceptable cost-effectiveness. SNRB was not cost-effective even when the societal savings of earlier return to work were included. The use of SNRB for suspected multilevel nerve root compression was less cost-effective. A range of probabilistic and deterministic sensitivity analyses confirmed that SNRB was unlikely to be a cost-effective method for diagnosis and planning surgical therapy. However, our conclusions were sensitive to assumptions about the continuing clinical effectiveness and cost savings of surgery beyond 1 year. Under the optimistic assumption that the economic benefits of surgery reported by RCTs at 1 year continue undiminished in subsequent years, then SNRB became cost-effective from the perspective of society, despite relatively poor diagnostic accuracy.

Discussion

There were few studies that estimated the diagnostic accuracy of SNRB in patients with low back pain and radiculopathy who have discordant or equivocal clinical and imaging findings. Research on this topic is hampered by the lack of a diagnostic gold standard against which to compare tests such as SNRB. We identified five diagnostic accuracy studies, all at high risk of bias. Of particular concern was the fact that many studies were at risk of verification bias as patients with a positive SNRB were more likely to undergo surgery (the reference standard) than those testing negative. There was substantial variation in estimates of sensitivity and specificity across studies; sensitivity ranged from 57% to 100% and specificity from 10% to 86%. Based on the two cohort studies that used post-surgery outcomes as the reference standard, the summary sensitivity was 93.3% (95% CI 85.8% to 97.0%) and summary specificity was 25.6% (95% CI 5.4% to 67.5%). However, conclusions based on these data should be tempered because of the large CIs around specificity and the high risk of bias which affects these studies.

Two previous SRs on the topic have been supportive of the diagnostic use of SNRB. The more recent review concluded that there was 'moderate evidence for SNRBs in the preoperative evaluation of patients with negative or inconclusive imaging studies, but with clinical findings of nerve root irritation'. Based on our review of the evidence, we believe that these conclusions are too strong. The differences in interpretation between our review and those conducted previously may be partly owing to our use of more rigorous eligibility criteria, restricting analysis to studies that provided sufficient data to construct estimates of sensitivity and specificity.

Despite case reports of serious adverse events associated with SNRB, our SR confirmed that these were very rare events. Of the seven studies identified that reported on complications and adverse events of SNRB ($n > 1500$ patients), no serious adverse events were reported. The largest case series reported minor and transient complications in 5.5% of patient visits, but no major or permanent complications.

Our economic model indicated that, in patients with suspected single-level nerve root compression, SNRB does increase the proportion of patients with an accurate diagnosis of the presence or absence of nerve root compression (59.5% vs 50%) and the proportion of patients with nerve root compression who undergo surgery (20.1% vs 18%). However, these benefits do not appear to be justified by the additional costs of testing. The incremental cost per additional case accurately diagnosed was £2674 and the incremental cost per QALY gained was £1,576,007. In comparison with other health interventions, reviewed by the National Institute for Health and Care Excellence on behalf of the NHS, this does not represent good value for money. This conclusion was the same for patients with suspected two-level nerve root compromise and was not altered in sensitivity analyses varying several key assumptions of the model, including prevalence, the diagnostic accuracy of SNRB and the impact of the SNRB result on the probability of performing surgery. The model was sensitive to assumptions about the long-term costs and benefits of surgery. If the residual improvement in quality of life (utility) scores and the savings in costs observed in the surgical arm of trials at 12 months post randomisation continues, rather than diminishes over time, then SNRB has the potential to be cost-effective, despite low specificity. However, we conclude that it is unlikely based on the current evidence that SNRB is a cost-effective method for informing the decision to operate in patients with low back and leg pain where there is doubt about the localisation of the lesion.

Conclusions

There were few studies that estimated the diagnostic accuracy of SNRB in patients with radiculopathy and discordant or equivocal imaging findings. All studies were limited by the difficulty of making a reference standard diagnosis in all patients who were tested. The evidence that is available suggests that the specificity of SNRB is relatively low. Therefore, based on current weak evidence, it is unlikely that SNRB is a cost-effective method for determining which patients will benefit from lumbar surgery.

Implications for service provision

Our review highlights the uncertain value of SNRBs when used for diagnostic purposes to establish whether or not clinical symptoms result from a particular nerve root. However, the distinction between diagnostic and therapeutic SNRBs is often not straightforward. Many centres combine local anaesthetic and periradicular steroid injections in order to gain both diagnostic information and, potentially, longer-term pain relief for the patient. Evidence collated in SRs confirms that transforaminal epidural steroid injections can be an effective and cost-effective part of a treatment strategy for patients with radicular pain.

Better evidence is needed to inform practice in centres that currently rely on SNRB for diagnostic information to help decide whether, or at which level, to perform lumbar decompressive surgery. These centres could perform SNRB procedures as part of research projects to improve the evidence base.

Suggested research priorities

Our recommendations for future research are:

1. A large rigorous diagnostic cohort study to determine the diagnostic accuracy of SNRB in predicting the short-term outcome of lumbar surgery in patients with suspected radiculopathy but equivocal or discordant clinical and radiological findings.
2. Separate or nested diagnostic cohort studies to identify the optimal SNRB technique (e.g. optimal anaesthetic dose, the value of needle provocation and control injections at adjacent sites).

3. A RCT to measure the impact of diagnostic SNRB on treatment decisions and the costs and outcomes of care for (subgroups of) patients with discordant or equivocal clinical and imaging findings of nerve root compression.

Funding

Chapter 1 Background

Prevalence and cost of low back pain

On any single day, 15–19% of adults in the UK report symptoms of low back pain.[1,2] During each year 36–48% of adults recall having low back pain[1–3] and 58–62% of the people will have low back pain at some point in their lives.[2–4] The economic burden of back pain in the UK, including health-care costs and lost productivity, is approximately £12B.[5] In most acute cases seen in primary care the pain is limited to the lower back and will resolve after a few days or weeks. However, some patients develop chronic pain and disability.[6] Others have referred symptoms of pain, sensory disturbance (e.g. numbness) and weakness in the leg. In a small group of patients with low back pain, the underlying cause of symptoms is lumbar radiculopathy (LR), and this can be due to inflammation or compression of a spinal nerve root.

Frequency of lumbar decompressive surgery, clinical effectiveness and cost-effectiveness

Substantial numbers of patients with persistent low back pain are treated surgically. In 2009–10 there were >9300 primary excisions of a lumbar intervertebral disc performed on NHS inpatients in England. A further 12,500 patients underwent other primary decompression operations on the lumbar spine.[7]

Randomised trial evidence on the clinical effectiveness and cost-effectiveness of lumbar decompressive surgery in patients with radiculopathy and intervertebral disc herniation is not definitive. A recent systematic review (SR) of the topic identified five randomised controlled trials (RCTs) comparing surgery with conservative care ($n = 4$) or epidural injections ($n = 1$).[8] The review authors did not pool trial results in a meta-analysis because of clinical heterogeneity and poor reporting of data. One Dutch RCT, considered by the review authors to be at low risk of bias, randomised 283 patients who had had severe sciatica for 6–12 weeks and radiologically confirmed disc herniation to early lumbar discectomy (within 2 weeks) or prolonged conservative treatment with surgery if needed.[9,10] This trial concluded that surgery led to faster pain relief (2 and 8 weeks post randomisation), but there were no differences between the groups after 1 year. Another trial conducted in the USA, also considered to be at low risk of bias, randomised 501 patients with persistent radiculopathy and imaging evidence of lumbar disc herniation (LDH) to open discectomy or non-operative care.[11] The intention-to-treat analysis showed no statistically significant differences in any of the primary outcome measures, but there was considerable crossover between the randomly assigned groups. Interpretation of the trial was thus hampered by substantial non-compliance with treatment allocation (57% of patients randomised to surgery received it within 6 months, whereas 39% of patients randomised to non-operative care also received surgery within 6 months).

Cost–utility analysis conducted alongside the Dutch trial suggested that the cost of surgery was not offset by reductions in other health services resulting in net additional health service costs of €1819 (or £1449).[12] Nevertheless, the early surgery group experienced a greater increase in quality-adjusted life-years (QALYs) owing to faster relief of symptoms, and the cost per QALY gained of surgery was €41,000 (approximately £32,930). Given that the National Institute for Health and Care Excellence (NICE) threshold for defining cost-effective use of health service money is £20,000–30,000 per QALY,[13] the economic case for surgery seems finely balanced. However, the Dutch trial found that if the productivity savings and other non-health-care costs are factored into the economic analysis, early surgery becomes marginally cost-saving and probably cost-effective from the perspective of society.

Observational work demonstrates that the pain, function and mental health status of patients with LR improves significantly after lumbar discectomy.[14] However, surgery is not universally successful. In the

Maine Lumbar Spine Study, only 70% of surgically treated patients reported improved pain, 63% were satisfied with the outcome and 19% had had at least one reoperation at 5-year follow-up.[15] In 2009–10 there was one revision lumbar discectomy for every nine primary lumbar discectomies performed on NHS patients.[7] Improved diagnosis could help identify patients most likely to benefit from surgery and minimise the cost and risks associated with unsuccessful back surgery.

Diagnosis of the cause of low back pain and radicular symptoms

A timely and accurate diagnosis of the cause of low back pain is important, as it is occasionally an early symptom of a serious systemic disease or more complex spinal disease including tumour and infection.[16] However, the exact cause of low back pain is often difficult to diagnose. The distinction between radiculopathy and other types of referred lumbar spine pain is crucial for treatment planning. Radiculopathy is almost always caused by inflammation and/or compression of a nerve root, and the most common causes of compression are herniation of an intervertebral disc or stenosis of the lumbar canal usually in the lateral recess or occasionally in the neural foramen. Patients with compressive radiculopathy stand to benefit the most from surgical decompression of the nerve root (e.g. lumbar discectomy).

In most patients, the diagnosis of radiculopathy is made by careful correlation of clinical signs and symptoms (e.g. pain distribution, paresis, straight leg raising test) and imaging findings [e.g. evidence of disc herniation and nerve root compression on magnetic resonance imaging (MRI) or computed tomography (CT) scanning]. Neither clinical findings[17] nor radiological imaging have perfect diagnostic accuracy. Patients often find it difficult to define the boundaries of their leg pain, sensory disturbance or weakness. MRI studies on volunteers have demonstrated surprisingly high rates of asymptomatic disc protrusions and extrusions with associated nerve root compression.[18] Therefore, clinical and imaging evidence of nerve root compression may not be concordant. In a prospective study of patients with clinical findings of low back pain without lower limb symptoms ($n = 150$) or with LR ($n = 96$), Modic et al.[19] found MRI evidence of nerve root compression in both groups (27% of low back pain patients and 46% of radiculopathy patients). Diagnosis may be further complicated in the subgroup of patients who have nerve root anomalies[20] or bony malformations of the lumbosacral junction.[21] For patients with suspected LR in whom the clinical and imaging findings are equivocal or discordant, diagnostic uncertainty remains about the nature and source of the symptoms and, therefore, whether or not the patient is a good candidate for surgery to decompress the lumbar nerve root. In these cases, additional diagnostic tests such as selective nerve root blocks (SNRBs) could help clinicians and patients to choose between surgical and conservative care.

Diagnostic selective nerve root blocks

Selective nerve root blocks have been employed since the 1930s as a method of confirming the source of radicular pain prior to surgery.[22] Diagnostic SNRB consists of injection of local anaesthetic (e.g. 1 ml of 2% lidocaine) or other substances (e.g. corticosteroids) around a spinal nerve under imaging guidance. Both provocative responses (replicating the patient's symptoms during needle placement) and analgesic responses (significant reduction of symptoms after injection of anaesthetic) to SNRB may be diagnostically useful in confirming or ruling out a nerve root as the source of clinical symptoms. The diagnostic role of SNRBs has narrowed with the advent of imaging techniques such as MRI, which depict in exquisite detail the bony and soft tissue structures of the lumbar spine. Nevertheless, SNRBs are still used to identify the putative symptomatic nerve root in patients with probable radicular pain that is not fully concordant with the radiological findings or who have nerve root anomalies or transitional vertebrae.[23] Recent international consensus statements have concluded that properly performed diagnostic SNRBs '…are useful when the location of symptoms seems to conflict with abnormalities identified with imaging findings…',[24] although the evidence on this topic was categorised as being of only moderate quality. The diagnostic value of SNRB

should be weighed against the costs and the small risk of complications associated with the procedure such as leg weakness or exacerbation of pain.[25] Very rarely, there have been case reports of more serious complications, such as paraplegia.[26]

The diagnostic accuracy of selective nerve root blocks

Researchers have evaluated the diagnostic role of SNRB for >30 years.[27,28] However, many of the early studies are more correctly described as 'technical performance' rather than 'diagnostic accuracy' studies. Technical performance studies evaluate the most valid processes for performing SNRB (e.g. amount of anaesthetic used or positioning of needle tip) rather than formal measures of diagnostic accuracy such as sensitivity or specificity. The diagnostic accuracy of SNRB is difficult to evaluate because of a lack of an obvious reference standard against which to compare it.

Studies have used either a diagnostic within-patient case–control design or a diagnostic cohort design to evaluate the diagnostic accuracy of SNRB. In the within-patient case–control design, patients have clear clinical signs of radiculopathy and imaging findings of nerve root compression at the corresponding lumbar spine level. These patients are given a SNRB at that 'case' level in the expectation that, if the test is sensitive, then radicular symptoms will be temporarily relieved by the anaesthetic. A 'control' injection is also performed on the same patient at a different site in the lumbar spine (e.g. an adjacent nerve root), in the expectation that, if the test is specific, the control injection will not affect radicular symptoms. Standard case–control studies are criticised for inducing spectrum bias as the cases and controls are considered not to be representative of patients in whom SNRB would be used in actual practice.[29] This criticism also applies to the within-patient case–control design, in which patients are selected based on concordance between clinical and imaging findings. In practice, in patients who receive SNRB, there is likely to be some discordance in the clinical and MRI findings.

In the diagnostic cohort study design, a group of patients with suspected radiculopathy undergo the index test (SNRB) and the result of this index test is compared with a reference standard. For LR, the reference standard is usually some combination of surgical findings, surgical outcomes and outcomes of conservative care. All of these standards fall well short of being a gold standard (e.g. a poor surgical outcome might result from poor surgical technique rather than incorrect diagnosis of radiculopathy).

The potential therapeutic impact and cost-effectiveness of selective nerve root blocks

Lumbar spine nerve root injections with 'therapeutic' rather than 'diagnostic' intent may have an effect on reducing leg pain and the proportion of patients who eventually have surgery.[30] A SR of the topic, conducted in 2009, including nine RCTs, concluded that there is fair evidence that transforaminal epidural steroid injections are superior to placebo for treating radicular symptoms and good evidence that these injections can be used to avoid surgery.[31] However, the independent role of the anaesthetic and the steroid in this overall treatment effect is less clear. A double-blinded RCT comparing up to four nerve root injections using either anaesthetic alone (1 ml of 0.25% bupivacaine) or anaesthetic plus steroid [1 ml betamethasone (6 mg/ml)] in 55 patients with lumbar radicular pain found that the addition of betamethasone increased the proportion of patients deciding not to have surgery from 33% to 71% ($p < 0.01$).[32] A further publication on this study followed up the patients who had avoided surgery for 5 years and found that the majority of patients who avoided an operation for at least 1 year after receiving a nerve root injection with bupivacaine alone or in combination with betamethasone continued to avoid operative intervention for a minimum of 5 years.[33] Conversely, a larger ($n = 150$) double-blind RCT conducted in the UK randomised patients with unilateral leg pain and MRI-confirmed nerve root compromise to receive 2 ml of 0.25% bupivacaine alone or with 40 mg of methylprednisolone (Depomedrone®, Pfizer). The trial found no significant differences between groups in Oswestry Disability

Index or leg pain visual analogue scale (VAS) scores at 6 or 12 weeks after randomisation. There was no strong evidence that rates of surgery at 1 year were different between the anaesthetic and anaesthetic plus corticosteroid arms (21.5% vs 14.1%; $p = 0.38$).[34]

The impact of 'diagnostic' SNRB results on treatment decisions is less well studied, but the potential for diagnostic and therapeutic impact is large. Primary excisions of lumbar intervertebral disc procedures involve a mean inpatient stay of 3.2 days, totalling 30,738 days in NHS hospitals in England annually.[7] This use of acute-care resources, combined with additional NHS costs and productivity losses associated with rehabilitation from surgery, suggest that a minimally invasive test that accurately differentiates patients who will or will not benefit from surgery has the potential to be cost-effective. However, in order to evaluate this, unbiased evidence on the diagnostic accuracy of SNRB, procedure-related complications and the impact of diagnosis on surgical management and the cost and outcomes of therapy should be combined in a formal decision analysis.

Chapter 2 Research questions

This evidence synthesis aimed to determine whether or not SNRBs result in more accurate diagnosis in patients considered for lumbar decompression surgery where there is doubt about the localisation of the lesion based on clinical signs and imaging findings (e.g. MRI). We developed an economic model to evaluate the extent to which improvements in diagnostic accuracy lead to more cost-effective care for this patient group and subgroups within it. Specifically, the project addressed the following objectives:

1. Conduct a SR to determine the diagnostic performance of SNRB in patients with probable radicular pain that is not fully concordant with the imaging findings prior to lumbar decompression surgery.
2. Evaluate whether or not the diagnostic accuracy of SNRB varies by patient subgroups (e.g. patients with suspected radiculopathy at more than one level of the lumbar spine).
3. Conduct a SR to summarise the evidence on the incidence of procedure-related complications of diagnostic SNRB.
4. Conduct a SR of previous economic studies of the use of SNRB in patients with suspected LR and develop a cost-effectiveness model to evaluate the cost-effectiveness of using SNRB in patients with discordant clinical and imaging findings, including value of information analysis.

Chapter 3 Systematic review methods

Search strategy

Studies were identified by searching the following databases from inception to 18 August 2011: MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, EMBASE, Science Citation Index, Bioscience Information Service (BIOSIS) and Latin American and Caribbean Health Sciences Literature (LILACS). In addition, information on studies in progress, unpublished research or research reported in the grey literature was sought from a range of relevant databases including Inside Conferences, Dissertation Abstracts and National Technical Information Service (NTIS). We combined terms for SNRB [e.g. 'exp Nerve Block/' or '(nerve adj3 block$).tw.' or 'SNRB.tw.' or '(neural adj3 block$).tw.' or '(nerve adj3 injection$).tw.' or '(nerve adj3 infiltration).tw.'] with terms for the target condition [e.g. 'radiculopath$.tw.' or 'radiculitis. tw.' or '(radicular adj3 pain).tw.' or 'Sciatica/' or sciatica.tw.']. We did not use a methodological search filter to identify diagnostic accuracy studies as such filters result in the omission of relevant studies.[35,36] There was no restriction of study by country of origin, language or publication date. Attempts were made to identify further studies by examining the reference lists of all retrieved articles and previous reviews. Full details of the search strategies and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist are given in *Appendices 1* and *2,* respectively.

Inclusion and exclusion criteria

Two reviewers independently screened titles and abstracts for relevance to any of the three SRs: any disagreements were resolved by consensus or referral to a third reviewer. The full text of potentially relevant studies was obtained and assessed for inclusion by one reviewer and checked by a second. Full-text articles were also assessed for inclusion in the review of economic evaluations by a health economist. Articles were selected according to the criteria in *Table 1*. In cases where we were unable to extract 2×2 tables of test performance from otherwise eligible diagnostic accuracy studies, we contacted study authors to request this information.

Data extraction

Data extraction was performed by one reviewer and checked by a second. Microsoft Access (Microsoft Corporation, Redmond, WA, USA) data extraction forms were developed and piloted on two studies. The following data were extracted, where reported: study details (identifier, study design, location); participant details (age, sex, previous surgery, duration of radicular symptoms, inclusion criteria); SNRB details (criteria for a positive test, needle gauge, site of injection, anaesthetic name and dose, corticosteroid name and dose, method of imaging guidance, contrast agent, lumbar levels evaluated); and reference standard details (if applicable) (intraoperative findings, outcome after follow-up or other). For diagnostic accuracy studies we extracted 2×2 data on test performance [i.e. number of true-positives (TPs), false-negatives (FNs), false-positives (FPs), true-negatives (TNs)]. For studies of adverse events, we extracted data on the type, number, severity and duration (acute/chronic) of adverse events. Data were extracted at the patient level, unless unavailable, and then injection level was used.

TABLE 1 Inclusion criteria for each SR

	Review of diagnostic accuracy	Review of procedure related complications	Review of economic evaluations
Population	Patients with low back pain and symptoms in a lower limb		
Target condition	LR		
Index test	Diagnostic SNRB administered under radiological guidance		
Reference standard	Any reported reference standard, e.g. surgical findings and/or clinical outcomes	N/A	N/A
Outcome(s)	Sufficient data to construct 2×2 contingency tables	Transient and permanent adverse events	Cost-effectiveness, cost–utility, cost–benefit, cost–consequence study
Study design	Diagnostic cohort or (within-patient) case–control studies	Any study design with at least 15 patients	RCTs, controlled studies, decision analyses

N/A, not applicable.

Quality assessment

Diagnostic accuracy studies were assessed for methodological quality using the quality assessment of diagnostic accuracy studies (QUADAS)-2 tool.[37] This tool assessed study quality in terms of risk of bias and concerns regarding applicability and includes domains covering patient selection, index test, reference standard and patient flow.

Bias occurs if the results of a study are distorted by systematic flaws or limitations in its design or conduct (e.g. knowledge of the index test result when interpreting the reference standard). Applicability may be reduced if patient demographic and clinical features, or the use or interpretation of the index test in the diagnostic accuracy study differ from those specified in the SR research question. Reviewers rate concerns regarding applicability and risk of bias as low, high or unclear.

The first section of QUADAS-2 asks reviewers to state their review question in terms of the relevant patient group, index test, target condition and reference standard(s). This is to aid with judgements of applicability – for example, if a study enrols a slightly different patient group, then it would be judged as having high concerns regarding applicability. We defined the review question for the diagnostic accuracy review as:

Patients Patients with low back pain and radiculopathy (or sciatica) with non-congruent imaging and clinical findings who might benefit from lumbar decompression surgery.

Index test SNRB including injection of anaesthetic close to the lumbar nerve root under guidance by fluoroscopy or other imaging.

Target condition Radiculopathy (or sciatica) amenable to surgery.

Reference standard Outcome following surgery.

Full details of the QUADAS-2 checklist, adapted for our review, are provided in *Appendix 3*. QUADAS-2 forms were developed in Microsoft Access. We did not formally assess the quality of studies of adverse events or economic evaluations. Quality assessment was carried independently by four reviewers and the responses compared. Disagreements were resolved through consensus.

Data analysis

We calculated sensitivity and specificity together with 95% confidence intervals (CIs) for each set of 2×2 data. We plotted estimates of sensitivity and specificity from individual studies in summary receiver operating characteristic space. For the cohort studies, we estimated summary sensitivity and specificity together with associated CIs using univariate logistic regression random-effects meta-analysis. There were insufficient data to allow use of the more statistically robust bivariate/hierarchical summary receiver operating characteristic models. Analyses were stratified according to whether findings at surgery or outcome following surgery were used as the reference standard. Owing to the small number of studies that assessed adverse events and economic evaluations, a narrative synthesis was used to combine findings.

Chapter 4 Results of the systematic review of diagnostic accuracy

Details of included studies

The searches identified 11,211 titles and abstracts; of these, 138 were considered potentially relevant, retrieved and screened as full papers and five studies ($n = 241$ patients; range 15–83 per study) were included (see *Appendix 5* and *Figure 1*). Details of studies excluded following full-paper screening are included in *Appendix 4*.

Two studies were within-patient case–control studies,[38,39] one was a prospective diagnostic cohort study[28] and two were retrospective diagnostic cohort studies[40,41] (*Table 2*). Publication dates ranged from 1973 to 2008. All studies were conducted in secondary care and enrolled small numbers of patients (range 15–83 patients). Where reported, the mean age of patients ranged from 46 to 47 years, the majority were male, most had experienced symptoms for at least 3 months, and the proportion who had undergone previous surgery ranged from 0% to 48%.

The two within-patient case–control studies confirmed the symptomatic nerve root in all enrolled patients by concordant clinical and radiological or surgical findings prior to the use of SNRB. The specificity of SNRB in these two studies was evaluated through control injections; in the Yeom *et al.*[38] study these were given at adjacent asymptomatic nerve roots, whereas in the North *et al.*[39] study three other anatomical sites in the lumbar spine were injected (sciatic nerve, facet joint and subcutaneous). However, North *et al.*[39] present diagnostic accuracy data based only on the control injection at the sciatic nerve, and the other two control injection sites are not considered further in this review. The three diagnostic cohort studies recruited patients with suspected LR where some doubt remained because of equivocal or discordant clinical and radiological findings. These studies used intraoperative findings and/or outcome following surgery as reference standards.

Details of the injections used in the included studies are given in *Table 3*. The type of local anaesthetic given differed between studies (lidocaine, bupivacaine, procaine or mepivacaine), with doses ranging
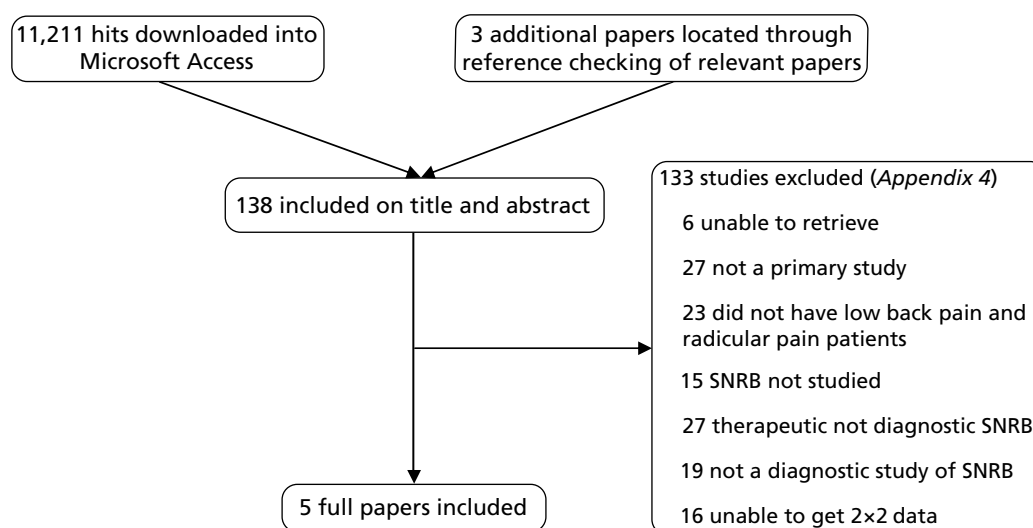
FIGURE 1 Flow chart of study selection process.

TABLE 2 Included study baseline details

Author (year), country	n analysed/ n recruited	Inclusion criteria	Exclusion criteria	Description of included patients	Details of previous surgery	Mean age (years)	% male	Recruitment years	Mean symptom duration (range)
Within patient case–control studies									
Yeom[38] (2008), NR	47/83	Patients who were to undergo a lumbar spine operation with single-level, unilateral lumbosacral radiculopathy confirmed by clinical, radiographic and MRI findings	Multilevel or bilateral neural compression on MRI, prolonged pain relief after first injection that precluded evaluation of next block; operations cancelled because of persistent pain relief after SNRB	Patients with established pure radiculopathy from a single level. Affected roots were L4 in 3, L5 in 31, S1 in 13. Concordant imaging and clinical findings	No history of lumbar surgeries	47 (18–76)	60	2005–6	3 months (15 days–3 years)
North[39] (1996), USA	33/33	Patients with sciatica with or without low back pain, attributed to spinal pathology	Active issues of secondary gain or compensation; prominent signs of somatisation. Symptoms indicating a lesion in sciatic nerve or its branches, or piriformis entrapment	Established sciatica patients with or without low back pain. All had L5 or S1 radiculopathy. 52% had diagnostic imaging findings of ongoing nerve root compression. The remaining 48% had a well-documented history of root compression which had been corrected surgically	48% history of root compression corrected surgically	46 (24–70)	73	NR	>6 months

Prospective diagnostic cohort studies

Author (year), country	n analysed/n recruited	Inclusion criteria	Exclusion criteria	Description of included patients	Details of previous surgery	Mean age (years)	% male	Recruitment years	Mean symptom duration (range)
Schutz[28] (1973), Canada	15/23	Patients with current sciatica	NR	Patients with sciatica. Investigation undertaken only at a time when sciatica symptoms actually present	One patient had previous surgery, unsuccessful SNRB and excluded from analysis. Unclear if patients included in analysis had previous surgeries	NR	NR	NR	NR

Retrospective diagnostic cohort studies

Author (year), country	n analysed/n recruited	Inclusion criteria	Exclusion criteria	Description of included patients	Details of previous surgery	Mean age (years)	% male	Recruitment years	Mean symptom duration (range)
Sasso[40] (2005), USA	83/83	Patients who underwent selective nerve root injections, MRI and nerve root decompression surgery and had a follow-up evaluation >12 months post surgery	NR	Patients with cervical or LR. Discordant imaging and clinical findings	Unclear how many previous lumbar surgeries. Twenty patients with cervical or lumbar symptoms had previous surgery [15 patients at same and/or adjacent level(s) and five patients at non-adjacent levels]	NR	NR	1996–9	4.7 months (1.5–27)
Dooley[41] (1988), Canada	62/73	Patients who underwent NRI	NR	Patients with radicular pain who underwent NRI	32 patients with one or more previous surgeries. Three patients had four surgeries	NR	NR	1982–3	NR

NR, not reported; NRI, nerve root infiltration.

from 1 ml to 3 ml: none of the studies combined the anaesthetic with a steroid. Four studies reported using fluoroscopic guidance for needle placement;[38–41] one study did not specify the guidance method.[28] Four studies reported using a contrast agent.[28,38,40,41] Needle provocation of the nerve root was conducted in four studies.[28,38,40,41] Similarly, three studies[28,38,39] carried out up to three control injections at adjacent asymptomatic levels (two[38,39] being the within-patient case–control studies). The third[28] used the control injections in order to try to increase the sensitivity and specificity of patient responses to injections at the level thought to be symptomatic. Post-procedure assessment of pain response was often not well described and varied from immediate pain relief to detailed assessment every 15 minutes for the first 3 hours.

There was no consistency in the degree of post-test pain relief, which was defined as indicating a positive SNRB result (see *Table 5*). Three studies[28,38,39] used a quantification of pain relief ranging from 50% relief to 100% relief. Sasso *et al*.[40] defined a positive SNRB as a post-injection visual analogue scale (VAS; 0–10) pain score of 0 or 1 and immediate relief of >95% of the patient's extremity pain, even when pain-provoking manoeuvres were performed. Dooley *et al*.[41] reported response to SNRB in four groups based on all four permutations of whether or not typical pain had been recreated when the needle was inserted (yes/no) and whether or not the complete pain relief was achieved after injection of anaesthetic (yes/no). Data from this study can, therefore, be combined in different ways giving results at each threshold. We selected patients who had either a group 1 (typical pain on needle insertion and relief of pain following SNRB) or a group 3 (no typical pain on needle insertion, but relief of pain following SNRB) response as our threshold for a positive test. This definition is most similar to the other studies that did not use pre-injection pain provocation when interpreting the index test result; it is also most applicable to centres that do not perform needle provocation, relying solely on the response to anaesthesia to reach a diagnosis.

Two studies[28,41] used intraoperative findings as the reference standard (see *Table 5*). One of these studies[41] also used outcome following surgery as a second reference standard. Sasso *et al*.[40] used outcome at 12 months following surgery. The two within-patient case–control studies used concordant symptoms and imaging evidence of nerve root compression (or lack of) as the reference standard for injections given at the symptomatic (or adjacent) sites.

Quality of included studies

All studies were judged to be at high risk of bias on two or more domains (*Table 4*). All studies were judged to be at high risk of bias for reference standard, the three cohort studies[28,40,41] were at high risk of bias for flow and timing and the two within-patient case–control studies[38,39] were at high risk of bias for patient selection. Two cohort studies[40,41] were judged as low concerns regarding applicability on all domains. There were high concerns regarding the applicability of the third cohort study[28] as the reference standard consisted of intraoperative findings alone. Both within patient case–control studies[38,39] were judged as high concerns regarding applicability for patient selection. *Figure 2* shows the proportions of studies rated as having a high, low or unclear risk of bias or concerns regarding applicability for each domain (patient selection, index test, reference standard, and flow and timing).

Patient selection

Two cohort studies[40,41] were judged to be at low risk of bias as they enrolled patients with low back pain and radiculopathy in whom the radiculopathy level was not confirmed, with no further restriction. The third cohort study[28] was judged to be at unclear risk of bias as it did not provide details on how patients were selected. The two within-patient case–control studies[38,39] enrolled patients with clinically and radiologically confirmed radiculopathy from a single level and so were judged to be at high risk of bias.

There were high concerns regarding applicability for the two within-patient case–control studies[38,39] because the included patients did not have discordant imaging and clinical findings. One of the cohort

TABLE 3 Details of SNRB injections used in included studies

Author (year)	Clinician	Needle gauge	Needle position	Needle level	Anaesthetic name	Anaesthetic concentration	Anaesthetic dose	Steroid used	Guided method	Contrast agent used	Needle provocation	Control injections	Time to pain measurement	Time before surgery
Yeom[38] (2008)	Spinal radiologist	22	Neural foramen near target nerve root	L3, L4, L5, S1	Lidocaine	2%	1 ml	No	Fluoroscopy	Yes – 1 ml iohexol myelographic	No	1 or 2	30 minutes	1–2 days
North[39] (1996)	Individual with extensive experience	NR	Lumbosacral root at L5 or S1 foramen	L5, S1	Bupivacaine	0.5%	3 ml	NR	Fluoroscopy	NR	Yes	3	Every 15 minutes for 3 hours	NR
Schutz[28] (1973)	NR	NR	The superior level of the intervertebral foramen around the nerve root	L4, L5, S1	Procaine	NR	1 ml	NR	Guided but method NR	Yes – 1 ml ethodian	Yes	1 or 2	Immediate	NR
Sasso[40] (2005)	NR	22, 21 or 20	The anterosuperior aspect of the neuroforamen of the selected nerve root	NR	Lidocaine	2%	0.5–0.75 ml	NR	Fluoroscopy	Yes – 0.25–0.75 ml Iohexol	Yes	NR	Immediate	1–3 months
Dooley[41] (1988)	NR	18	The proximal end of the intravertebral foramen for lumbar nerve roots. Needle introduced vertically through the posterior foramen for the first sacral nerve root	L3, L4, L5, S1	Mepivacaine or lidocaine	1%	1 ml	NR	Fluoroscopy	Yes – ethyl iodophenyl undecylate	Yes	NR	Immediate	NR

NR, not reported.

studies[28] was judged as having unclear applicability, as the details on the included patients were limited. The other two diagnostic cohort studies[40,41] were judged as low concerns regarding applicability.

Index test

Four studies[29,39–41] were judged to be at low risk of bias. All three cohort studies[28,40,41] performed the SNRB before the reference standard was applied and one of the within-patient case–control studies[39] blinded patients to the nature of the individual blocks delivered and so test review bias could be ruled out; all studies[29,39–41] pre-specified the threshold for a positive SNRB test or provided a breakdown of individual patient results. The other within-patient case–control study[38] was judged to be at high risk of bias, despite blinding patients to the nature of the blocks, as it used the pain relief threshold with the highest diagnostic accuracy to determine a positive SNRB result, although sensitivity and specificity values at other thresholds were also reported.

All studies were judged as low concern regarding applicability as all diagnostic SNRBs were adequately described as being localised to the nerve root and administered under imaging guidance.

Reference standard

All of the reference standards used were imperfect. Intraoperative findings are sometimes equivocal. Decompression takes place in order to expose the nerve root and only the proximal part of the root is normally seen. Most decompression procedures in the lumbar spine involve the disc and lateral recess but rarely expose the nerve root in the foramen. If the surgeon is not blinded to the result of the SNRB, then the intraoperative judgement of nerve root compression is particularly susceptible to bias. A post-surgical outcome reference standard is also problematic as these outcomes will be affected by the technical quality of the surgical procedure and any concomitant therapy the patient has in the interim period between index test and reference standard. Therefore, a poor surgical outcome might not purely or even predominantly be the result of an incorrect diagnosis at SNRB. The within-patient case–control studies which use the concordant clinical and imaging findings at the 'case' and 'control' injection site will also be flawed if the clinical and imaging findings are both wrong. For these reasons, all reference standards applied in the included studies were judged to be at risk of bias. Furthermore, in all three cohort studies[28,40,41] the clinical or research teams were not blinded to the SNRB findings when recording the intraoperative or post-surgical outcomes.

We considered studies that used outcome following surgery as the reference standard to be most applicable, as this is the outcome of most importance to patients. The two cohort studies[40,41] that used this reference standard were, therefore, judged as low concerns regarding applicability.

Flow and timing

Verification bias was a major risk in all three cohort studies.[28,40,41] All three selected patients to undergo surgery based on the SNRB result, with patients testing positive more likely to receive surgery. It is likely that the patients with negative SNRB results who, despite this, were selected for surgery were a biased subset of those testing negative as these are likely to have been the patients in whom the clinicians suspected a FN result. One of the within-patient case–control studies[38] was also judged to be at high risk of bias for this domain, as 15 patients were excluded after the SNRB had been delivered and reasons for exclusion were not reported.

Summary of test accuracy results

The diagnostic cohort studies reported sensitivity and specificity based on per-patient analyses, whereas sensitivity and specificity from the within-patient case–control studies were based on per-injection analyses. There was substantial variation in estimates of sensitivity and specificity across studies: sensitivity ranged from 57% to 100% and specificity from 10% to 86% (*Table 5* and *Figure 3*). Most studies reported relatively high sensitivity (in excess of 87%), with the exception of that by Yeom *et al.*,[38] in which sensitivity
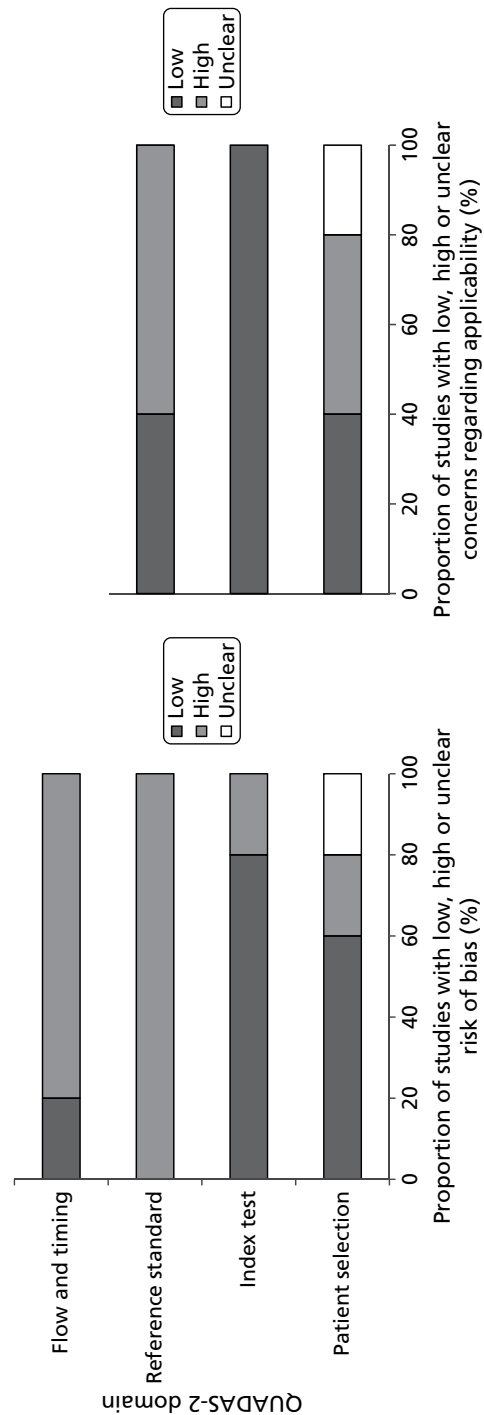
FIGURE 2 Proportion of included studies fulfilling each QUADAS-2 domain.

TABLE 4 Quality assessment of diagnostic accuracy studies-2 results

	Risk of bias				Applicability concerns		
Author (year)	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Within-patient case–control studies							
Yeom[38] (2008)	☹	☹	☹	☹	☹	☺	☹
North[39] (1996)	☹	☺	☹	☺	☹	☺	☹
Diagnostic cohort studies							
Sasso[40] (2005)	☺	☺	☹	☹	☺	☺	☺
Schutz[28] (1973)	?	☺	☹	☹	?	☺	☹
Dooley[41] (1988)	☺	☺	☹	☹	☺	☺	☺

☺, low risk/concern; ☹, high risk/concern; ?, unclear risk/concern.

was much lower (57%). A similar divergence was also observed for specificity, which was low (< 75%) in four studies,[28,39–41] but higher (86%) in the Yeom *et al*. study.[38] This was unlikely to be purely a threshold effect, as the 70% pain reduction threshold used by Yeom *et al*.[38] to define a positive SNRB result was lower than most of the other studies, which would be expected to increase sensitivity and decrease specificity, whereas the reverse was found.

Yeom *et al*.[38] were the only researchers not to include needle provocation prior to injection of anaesthetic. However, this also is unlikely to explain the lower sensitivity reported in their study; less stringent criteria for defining test positivity (i.e. not requiring pain to be reproduced on needle provocation) typically result in an increase in sensitivity. Nevertheless, it is possible that the provocation of nerve root pain during the procedure makes patients with genuine nerve root compression better able to judge any subsequent pain relief from the anaesthetic.

Interpretation of specificity was particularly hampered by verification bias in the cohort studies. Because surgeons were not blinded to the SNRB results, very few patients with negative test findings had surgery. Schutz *et al*.,[28] Sasso *et al*.[40] and Dooley *et al*.[41] contribute a total of just eight TN cases to the analyses. The higher specificity reported by Yeom *et al*.[38] could be a manifestation of patient selection bias as 'control' injections were performed at a level of the spine where the patients had no symptoms and no imaging findings suggestive of pathology.

Owing to the patient selection bias inherent in within-patient case–control designs we decided that it would be inappropriate to combine the results of these studies with those of the diagnostic cohort studies to give an overall estimate of the accuracy of SNRB. Based on differences in the type of control injection used in the two within-patient case–control studies[38,39] (see *Table 5*), we did not pool their results. Owing to the incomparability of the different reference standards used, we decided not to pool results of cohort studies that used different reference standards. Based on the two cohort studies[28,41] that used an intraoperative reference standard, the pooled sensitivity was 93.5% (95% CI 84.0% to 97.6%) and specificity was 50.0% (95% CI 16.8% to 83.2%); in contrast, for the two studies[40,41] that used post surgery as the reference standard the summary sensitivity was 93.3% (95% CI 85.8% to 97.0%) and summary specificity was 25.6% (95% CI 5.4% to 67.5%). In both cases, specificity was low, implying that a high proportion of patients without nerve root compression might still have a positive SNRB result. However, conclusions based on these data should be tempered because of the large CIs around specificity and the high risk of bias, which affected all three diagnostic cohort studies.[28,40,41]

TABLE 5 Diagnostic accuracy results

Author (year)	Threshold	Reference standard	TP	FN	Sensitivity (%) (95% CI)	TN	FP	Specificity (%) (95% CI)
Within-patient case–control studies[a]								
Yeom[38] (2008)	70% pain relief – several other thresholds also evaluated	Concordant symptoms and imaging evidence of nerve root compression (or lack thereof)	27	20	57 (43 to 70)	50	8	86 (75 to 93)
North[39] (1996)	50% reduction in baseline pain following block	Concordant symptoms and imaging evidence of nerve root compression (or lack thereof)	30	3	91 (76 to 97)	8	25	24 (12 to 41)
Diagnostic cohort studies								
Schutz[28] (1973)	100% pain relief. Full trunk flexion and straight leg raising possible	Intraoperative findings	12	0	100 (76 to 100)	1	2	33 (6 to 79)
Sasso[40] (2005)	VAS score 0–1 and immediate relief of >95% pain	Outcome 12 months following surgery	71	3	96 (89 to 99)	5	4	56 (27 to 81)
Dooley[41] (1988)	Pain relief	Intraoperative surgical confirmation of root pathology	46	4	92 (81 to 98)	2	1	67 (9 to 99)
		Outcome following surgery (follow-up range 24–36 months)	28	4	88 (71 to 96)	2	19	10 (1 to 30)

a Please note that the unit used in the within-patient case–control studies is number of injections and some patients had two control injections at adjacent levels in addition to the affected nerve; in all other studies it is number of patients.
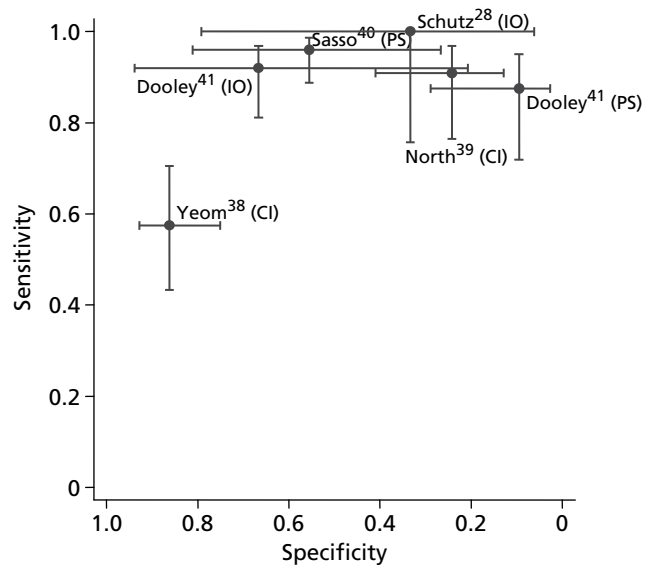
FIGURE 3 Receiver operating characteristic plot displaying diagnostic accuracy results of included studies. The CIs for sensitivity and specificity for each result are shown by the lines extending from the point estimates. CI, control injection reference standard; IO, intraoperative reference standard; PS, post-surgical reference standard.

None of the five included studies reported data on patients with suspected multiple nerve root compression separately from those with suspected single nerve root compression and, therefore, we were unable to perform a subgroup analysis on this group of patients.

Chapter 5 Review of complications of diagnostic selective nerve root block

Details of included studies

Seven studies[25,28,42–46] assessed complications and/or adverse events (see *Appendix 6* and *Table 6*). One study was a diagnostic cohort study,[28] one was a RCT[42] and five studies were case series.[25,43–46] Publication dates ranged from 1973 to 2010. Only one study[25] reported on the complications of SNRBs in the lumbar spine as the primary outcome of interest. This study included all patients ($n = 1203$) who received one or more therapeutic or diagnostic SNRBs in a radiology department with no details provided on their pre-test symptoms. The remaining six studies[28,42–46] were all conducted among participants with radicular pain in a lower limb but were generally small (15–117 participants analysed).

Table 7 gives full details of the SNRB injection methods and the adverse events reported. The needle gauge was reported in five[25,43–46] out of seven studies and ranged from 20 to 25. The needle length, reported in three studies,[43,45,46] ranged from 8 cm to 15 cm. Where reported, injected nerve root levels were L4–S1 in two studies[43,46] and L2–S1 in one study.[42] The local anaesthetic injected varied between the studies, anaesthetic volume ranged from 1 ml to 6 ml, and anaesthetic concentration, reported in five studies,[25,42,44–46] ranged from 0.25% to 1%. Three studies[25,44,46] used an injectable steroid as well as the anaesthetic. All SNRB procedures were guided and six studies[25,28,42,44–46] reported use of a contrast agent. Five of seven studies reported that there were no complications.[28,42–45] Tajima *et al*.[46] reported that '…pain in the lower extremity was aggravated for 1–2 days following selective radiculography and block in four patients. There was no other complication'. The largest study[25] reported that minor and transient complications were encountered in 98 of the 1777 total patient visits (during which 2217 injections were delivered to 1203 patients), giving an overall per patient visit complication rate of 5.5%. Complications occurred in 134 of the 2217 total injections (6% complication rate per injection). There were no major or permanent complications resulting from SNRB in this large case series. Stalcup *et al*.[25] also present data on the complication rate by needle tip position in an analysis limited to the patients who only received one SNRB. For needle tip positions that had been used in >50 injections, the complication rate ranged from 3.5% (7/199) to 7.4% (4/54) for needles placed in a posterior-superior-lateral position and an anterior-inferior-lateral position, respectively.

TABLE 6 Patient characteristics of studies reporting on adverse events following SNRB

Author (year), country	n recruited	n analysed	Inclusion criteria	Mean age (years)	% male
Case series					
Stalcup[25] (2006), USA	1203	1203	All adult patients who underwent a SNRB in the lumbar spine in the radiology department from 1 April 1997 to 31 May 2002	57.8	45
Ng[44] (2004), UK	125	117	Consecutive patients with clinical evidence of unilateral radicular pain that lasted despite at least 6 weeks of conservative management, MRI confirmation of nerve root compression secondary to LDH or peripheral degenerative spinal stenosis	52	52
Jonsson[43] (1988), Sweden	78	78	Patients with unilateral sciatic pain, severe enough for them to consider operation. Sciatic pain in one specific dermasome but with normal findings on myelography, CT and or MRI. Sciatic pain and minor radiographic findings according to myelography, CT or MRI. Pathological radiographic findings on multiple levels	44	34.6
Quinn[45] (1988), USA	33	33	Patients with a herniated disc ($n = 31$) or foraminal stenosis ($n = 2$) as identified by CT or MRI	NR	NR
Tajima[46] (1980), Japan	106	106	Patients undergoing lumbosacral radiculography and block who had lumbosacral diseases considered to be manifested by radicular symptoms	46	56
Prospective diagnostic cohort study					
Schutz[28] (1973), Canada[a]	23	15	Patients with current sciatica	NR	NR
RCT					
Ghahreman[42] (2010), Australia	150	27	Adult patients with pain radiating into the lower limb; associated with limitation of straight-leg raise to <30°; demonstration of a disc herniation by CT or MRI at a segmental level consistent with the clinical features. Pain of appropriate quality was the primary indication for treatment and surgery would be the next intervention if the injections did not relieve the pain. Only data for single arm of trial in which patients received anaesthetic was included in the current review	43	63

NR, not reported.
a Included in diagnostic accuracy SR.

TABLE 7 Injection details of studies reporting on adverse events following SNRB

Author (year)	Needle gauge	Needle length (cm)	Needle tip position	Needle levels	Anaesthetic name	Anaesthetic concentration (%)	Anaesthetic volume (ml)	Steroid used	Guided method	Contrast agent	Needle provocation used?	Adverse events
Stalcup[25] (2006)	22	NR	Adjacent or into the intervertebral foramen	NR	Bupivacaine	0.25	1–2	Yes – celestone (Betamethasone Sodium Phosphate, Betamethasone Acetate®, Shering-Plough) early in study, depomedrol later in study	Fluoroscopy	Yes	NR	Numbers given in injections: leg weakness n = 77 (3.5%); pain increased n = 51 (2.3%); other n = 6 (0.3%); total n = 134 (6.0%)
Ng[44] (2004)	22–25	NR	Superiorly to pedicle, medially to nerve and laterally to vertebral body	NR	Bupivacaine	0.25	2	Yes – methylprednisolone (Depo-medrone®, Pharmacia)	Assumed fluoroscopy	Yes	NR	No adverse events
Jonsson[43] (1988)	20	9	Just lateral to the opening of the intervertebral foramen	L4, L5, S1	Carbocaine	NR	3–6	NR	Fluoroscopy	NR	NR	No adverse events
Quinn[45] (1988)	22	9 or 15	An attempt was made to pierce the nerve or to have the needle tip within 1–2 mm of the nerve	NR	Lidocaine or bupivacaine	1 or 0.5, respectively	2.5–5	NR	CT	Yes	Yes	No adverse events

continued

TABLE 7 Injection details of studies reporting on adverse events following SNRB (*continued*)

Author (year)	Needle gauge	Needle length (cm)	Needle tip position	Needle levels	Anaesthetic name	Anaesthetic concentration (%)	Anaesthetic volume (ml)	Steroid used	Guided method	Contrast agent	Needle provocation used?	Adverse events
Schutz[28] (1973)[a]	NR	NR	Superior level of intervertebral foramen. Introduced about 2 inches from the midline	NR	Procaine	NR	1	NR	Guided but method NR	Yes	Yes	No adverse events
Ghahreman[42] (2010)	NR	NR	Placed in the intervertebral foramen of the target level	L2, L3, L4, L5, S1	Bupivacaine	0.5	2	No (steroid used in different randomised group)	Assumed fluoroscopy	Yes	NR	No complications occurred that could be attributed to the treatment
Tajima[46] (1980)	21	8–10	Approximately 4 cm lateral to upper margin of lumbar spinous process corresponding to nerve root to be radiographed	L4, L5, S1	Lidocaine	1	3	Yes – water-soluble corticosteroid	Radiography	Yes	Yes	Pain in the lower extremity was aggravated for 1–2 days following selective radiculography and block in four patients. There was no other complication

NR, not reported.
a Included in diagnostic accuracy SR.

Chapter 6 Assessment of cost-effectiveness evidence

Review of existing cost-effectiveness evidence

The 138 titles and abstracts of studies selected by the reviewers as being potentially relevant (see *Figure 1*) were assessed for inclusion in the economic review. None of the studies met the inclusion criteria. We identified two studies evaluating the cost-effectiveness of other types of spinal nerve injections [zygapophyseal (facet) joint injections and medial branch (facet nerve joint) blocks].[47,48] Although these studies provide indirect evidence that diagnostic injections in the spine can influence the percentage of patients receiving surgery and the cost of care, they do not provide direct evidence on the cost-effectiveness of diagnostic SNRB in patients with LR. We therefore constructed an economic model based on evidence from our SR on the diagnostic accuracy of SNRB and the wider literature on the costs and outcomes of diagnosis and treatment of radiculopathy.

Model overview

Perspective
We calculated cost-effectiveness from the perspective of the NHS and personal social services (PSS). We subsequently broadened the analysis to the societal perspective by including patient expenses and the costs of lost productivity resulting from back and leg pain.

Patient groups
Two hypothetical patient groups were considered in our economic evaluation: (1) individuals with suspected single-level nerve root compression considered for lumbar decompression surgery where there were discordant clinical and imaging findings; and (2) individuals with suspected two-level nerve root compression where there were discordant clinical and imaging findings. Two decision-analytic models were developed to estimate the cost-effectiveness of diagnostic SNRB in these groups.

Intervention and comparator
The economic model consisted of two arms: those patients who received only imaging and clinical work-up and those patients who received an additional SNRB to assess whether or not their symptoms were related to nerve root compression.

Outcomes
The model estimated the incremental cost per correct diagnosis and per QALY of SNRB.

Model structure

In developing the models, we aimed for the best-practice principles suggested by Buxton *et al*.:[49] (1) the models were kept as simple as possible to aid understanding; (2) the presentation of methods and results was as transparent as possible; (3) the quality of all data used in the models was explicitly discussed; (4) uncertainty in the models was explored using probabilistic sensitivity analysis (PSA) where possible; and (5) the models were internally verified and validated against other models and epidemiological studies where possible.

The short-run model considered the incremental cost per correct diagnosis of SNRB. The model for patients with suspected single-level symptoms is depicted in *Figure 4*. The model combined estimates of sensitivity and specificity with the pre-test prevalence of nerve root compression to generate post-test probabilities of accurate diagnosis. The short-run model allows for a proportion of patients to undergo repeat SNRB examinations at the same level if the initial test results are equivocal or are thought to need confirmation. The second model, in patients in whom two-level nerve root compression is suspected, repeats the diagnostic pathway so that SNRB is performed at both levels regardless of the SNRB result at the first level tested.

There are four possible diagnostic outcomes following SNRB: (1) positive SNRB response in a patient with symptoms caused by nerve root compression at that level (TP); (2) positive SNRB response in a patient whose symptoms are not caused by nerve root compression at that level (FP); (3) negative SNRB response in a patient with symptoms not caused by nerve root compression at that level (TN); and (4) negative SNRB response in a patient with symptoms caused by nerve root compression at that level (FN). Patients who undergo SNRB at two levels to evaluate possible two-level nerve root compression will receive a correct overall diagnosis only if a correct diagnosis is made at both levels. If the diagnosis is incorrect at either level this is considered a false diagnosis (*Table 8*).

We assumed that the working diagnosis was nerve root compression, based on clinical and imaging findings. Therefore, in the absence of SNRB (i.e. the top branch of *Figure 4*) this would be either a TP or FP diagnosis. Patients with suspected two-level nerve root compression who did not undergo SNRB have a TP diagnosis only if in fact they have nerve root compression at both levels. Otherwise, the working diagnosis is considered to be FP.

The long-term phase of the model estimated the costs and health effects of SNRB post diagnosis and treatment (*Figures 5* and *6*). This element of the model tracks patients as they have surgery or conservative care, as they incur costs and as their health-related quality of life evolves. Not all patients with positive SNRB results will go on to have lumbar spine surgery to decompress the nerve root. Patients may decline surgery because of resolving pain or despite ongoing pain if they prefer to continue with conservative care. Patients with negative SNRB results will also not necessarily avoid surgery. Surgery to decompress the nerve root investigated by SNRB might be pursued, despite the negative SNRB result, if persistent symptoms and imaging findings convince the clinician and patient that surgery is worthwhile.

For patients with suspected two-level compression, the diagnostic nerve root block may inform both the decision to perform surgery and the level(s) at which the surgery will be performed (see *Figure 6*). In these patients it is possible for the overall diagnostic result to be incorrect but the impact on the decision to perform surgery to be correct. For example, a patient who has a FP SNRB result on nerve root 'A' and a TP SNRB finding on nerve root 'B' would be more likely to undergo surgery to decompress both nerve roots. Therefore, the patient does undergo decompressive surgery on the symptomatic nerve root, which should relieve symptoms, albeit the surgery is more extensive than it need be because a second nerve root is also decompressed. A full description of each permutation of diagnostic result and the likely impact on the decision to perform surgery is provided in *Table 8*.

The long-term model (see *Figures 5* and *6*) estimated the initial costs and outcomes of care in the first year after diagnosis and treatment based on RCT evidence on the costs and outcomes of surgery and conservative care. After the first year, subsequent costs and utility (health-related quality-of-life) scores for patients were extrapolated over a period of 20 years using a two-state Markov process (recovering from low back pain and radiculopathy or death). Although evidence suggests that the majority of the benefits of surgery occur within the first year, this extrapolation allows us to estimate any residual benefits after 1 year and estimate QALYs as the cohort ages.
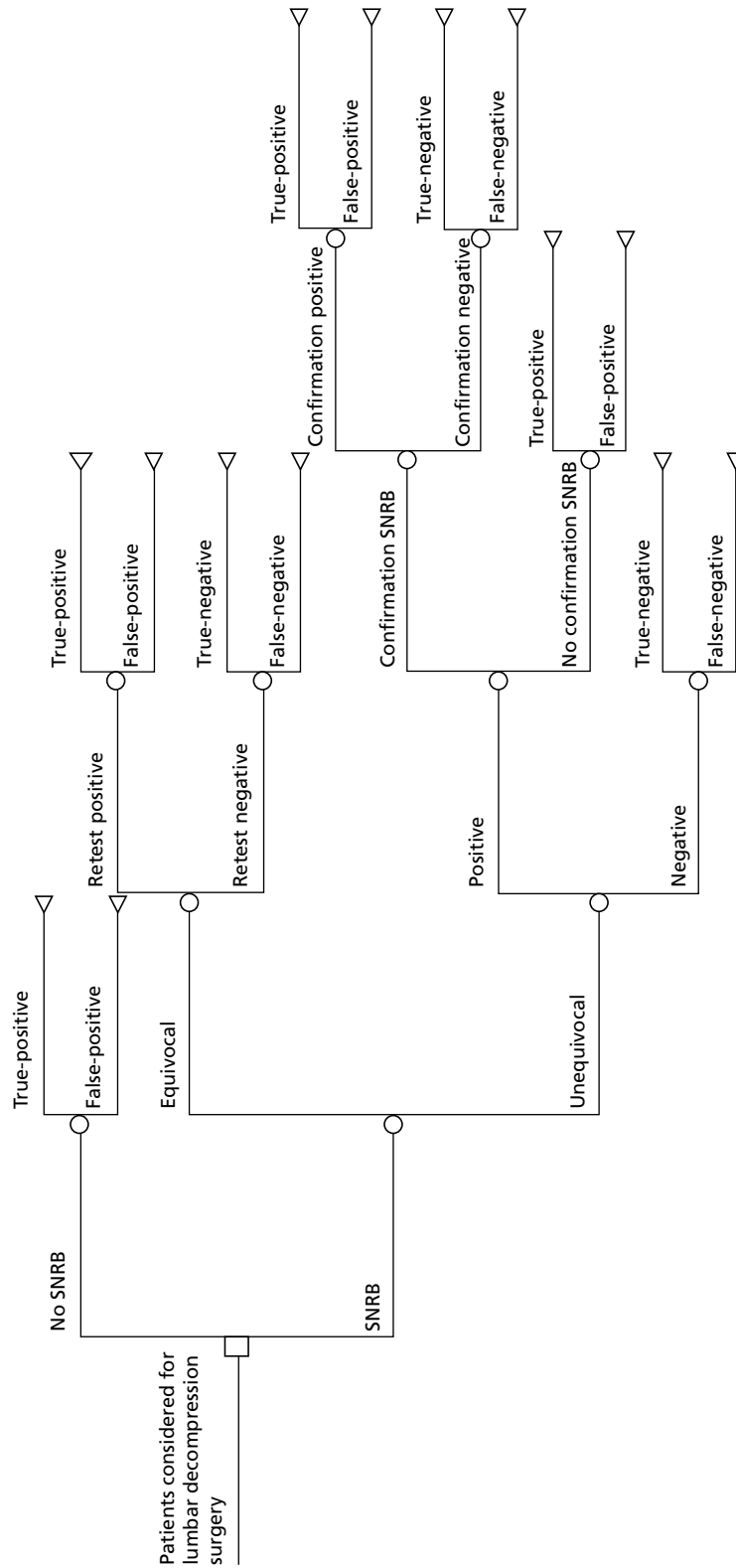
FIGURE 4 Model: incremental cost per correct diagnosis, suspected single-level nerve root compression. For patients with suspected two-level nerve root compression, the diagnostic pathway is repeated, so a patient may end up with any permutation of the four diagnostic results at the two levels investigated.

TABLE 8 Overall diagnostic and therapeutic outcome in patients with SNRB at two levels

Nerve root A	Nerve root B	Overall diagnostic result	Impact on decision to perform surgery	Explanation
FP	FP	False	FP	More likely to have surgery at two levels, both without NR compression
	TN	False	FP	More likely to have surgery at one level, without NR compression
	TP	False	TP	More likely to have surgery at two levels, one of which has NR compression
	FN	False	FP	More likely to have surgery at one level, but not the one that has NR compression
TN	TN	True	TN	More likely to have conservative care at both levels, without NR compression
	TP	True	TP	More likely to have surgery at one level, with NR compression
	FN	False	FN	More likely to have conservative care at both levels, one of which has NR compression
TP	TP	True	TP	More likely to have surgery at two levels, with NR compression
	FN	False	FN	More likely to have surgery at one level, but both levels have NR compression
FN	FN	False	FN	More likely to have conservative care at both levels, both of which have NR compression

NR, nerve root.

Model parameters

All model parameters are listed in *Table 9* and data sources for the parameters are described below.

Initial prevalence of nerve root compression

The prevalence of true nerve root compression is, to some extent, under the control of the clinician requesting the SNRB. Some clinicians may choose to use SNRB predominantly in patients whose symptoms they believe, based on clinical and imaging findings, are due to surgically amenable causes. In such a setting, prevalence will be low and the purpose of SNRB will be primarily to reassure the patient and clinician that surgery is not necessary. Alternatively, other clinicians may be more inclined to use SNRB as a final confirmatory test in patients whom they believe do have nerve root compression and will benefit from surgery. In this setting, the pre-test prevalence will be high. In order to take into account this variability in the use of SNRB, we conducted a deterministic sensitivity analysis (sensitivity analysis A) to evaluate the cost-effectiveness of SNRB at three levels of pre-test prevalence selected a priori: (1) a base-case moderate prevalence of nerve root compression (50%); (2) low prevalence of nerve root compression (25%); and (3) high prevalence of nerve root compression (75%). For patients with suspected two-level nerve root compression, the probability of compression at either level was assumed to be the same and these probabilities were assumed to be independent of each other.

Cost of the selective nerve root block diagnostic test

Our SR and broader searches identified no published sources on the cost of diagnostic SNRB injections. We therefore estimated the cost from NHS reference costs 2009–10 using the Healthcare Resource Group (HRG) codes' code of AB06Z 'minor pain procedure'.[50] SNRBs are generally performed on either a day-case or outpatient basis. We used the weighted average of outpatient and day case costs of £247 (see *Table 9*).
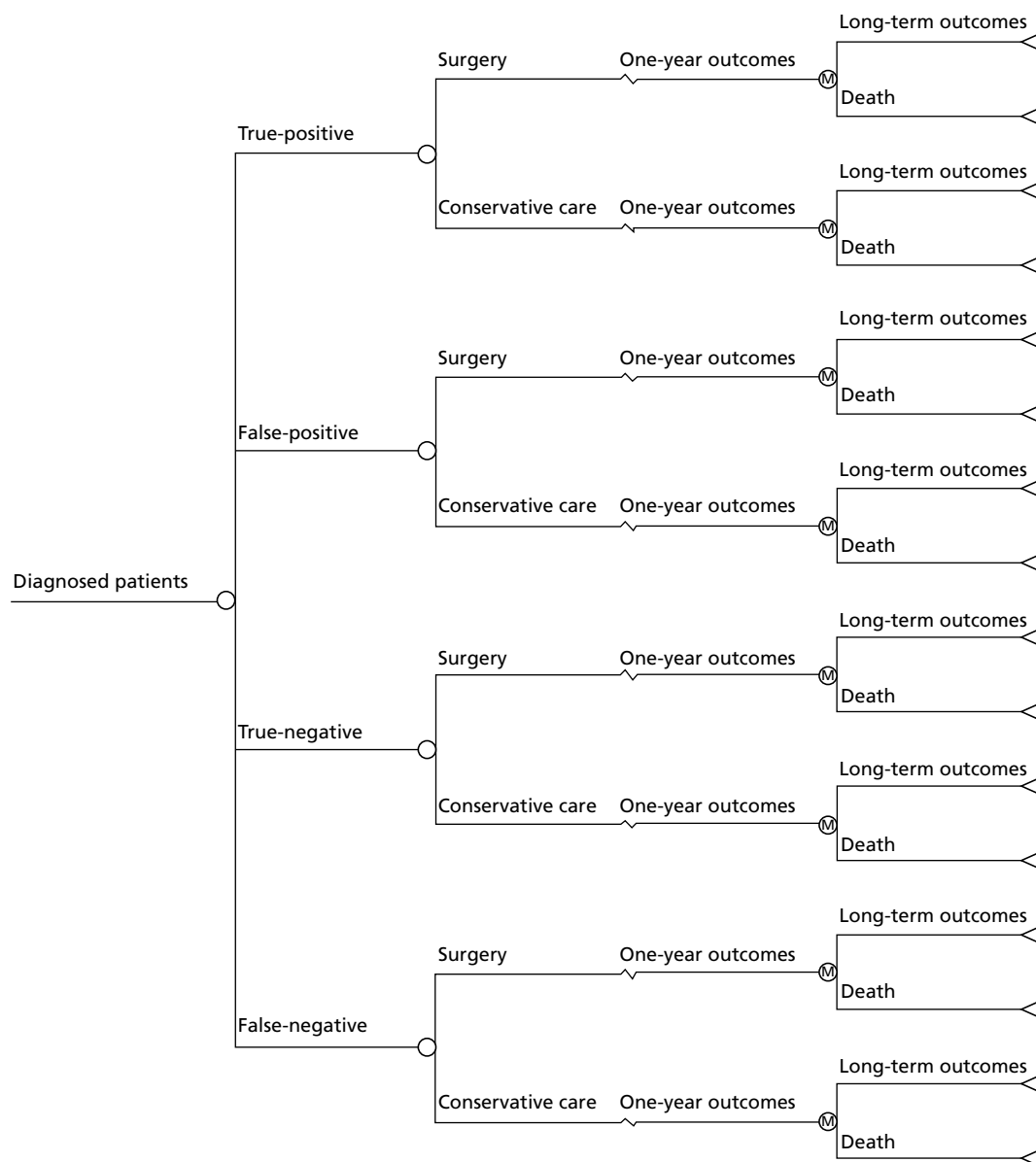
FIGURE 5 Diagnosis and treatment pathway – single-level nerve root compromise. Ⓜdenotes start of the Markov process.

The marginal cost of each additional SNRB was assumed to be identical to that of the initial SNRB as it typically requires a separate appointment.

The probability of selective nerve root block-related complications

Adverse events associated with diagnostic SNRB were reviewed as part of our SR. The largest study was conducted by Stalcup et al.[25] Although their study of 1777 patient visits found a 5.5% complication rate, the complications were minor and transient in nature. Given this, we decided not to model any quality-of-life decrements associated with these minor SNRB-related complications. However, very rarely case reports of much more serious complications are described in the literature.[26,51,52] We therefore included a small probability (1 in 10,000) of permanent paraplegia per SNRB injection. We assumed that, in this event, paralysis would occur immediately and reduce quality of life in the model to 51.6% of that of the treated group, adding a cost of £18,919 per year.[53]
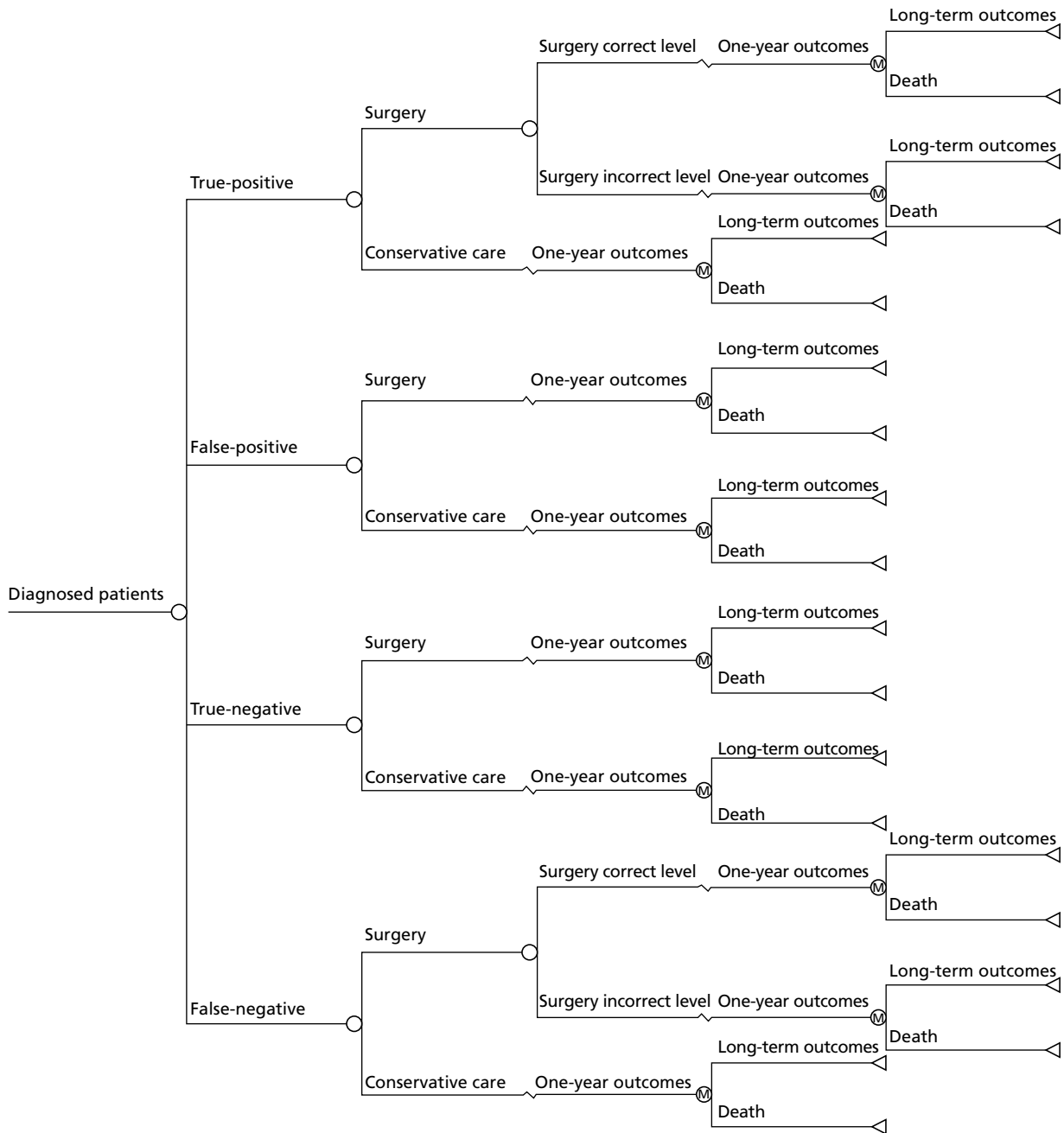
FIGURE 6 Diagnosis and treatment pathway – two-level nerve root compromise. Ⓜ denotes start of the Markov process.

The sensitivity and specificity of selective nerve root block

Sensitivity and specificity for the model were taken from our SR. We selected the pooled estimate of the two-cohort studies[40,41] that used post-surgery outcomes as the reference standard as this was considered to be the most applicable reference standard. In sensitivity analysis (sensitivity analysis B), we used estimates of diagnostic accuracy from two diagnostic accuracy studies to provide a representation of the range of high sensitivity/low specificity[40] and low sensitivity/high specificity[38] results that have been reported in the literature.

Likelihood of equivocal selective nerve root block results and repeating selective nerve root block on the same nerve root

Selective nerve root blocks are sometimes repeated at the same level when findings are equivocal, if the procedure was performed inadequately (i.e. incorrect needle positioning) or if continuing symptoms prompt reinvestigation of the same nerve root. The proportion of patients with equivocal SNRB tests was estimated from Sasso et al.,[40] where 6 of 573 patients had an equivocal initial SNRB and went on to receive a repeat SNRB at the same level. Of the 411 patients who had a positive finding at their initial SNRB, eight (1.9%) patients received a repeat confirmatory SNRB on the same nerve root. For individuals with a negative SNRB result at the initial level tested, none (0/156) received a repeat SNRB at the same level.

The impact of the selective nerve root block result on the decision to perform surgery

The same study by Sasso et al.[40] was the only one identified by our search that reported on the therapeutic impact of a positive and negative SNRB result on the probability of receiving surgery. Of the 573 patients, 433 patients had a positive SNRB result at one or more vertebral level (411 at the initial level tested and 22 at a subsequent level), of whom 21% (93/433) went on to receive decompression surgery at that level within 3 months. Of the 140 patients with equivocal or negative SNRB results, 8% (11/140) had decompression surgery at that level, despite the negative SNRB finding. We used these probabilities to estimate the likelihood of surgery after a positive or negative SNRB result. We assumed that the probability of surgery in the no SNRB arm would be the weighted average of the negative and positive SNRB probabilities [18% (104/573)].

The association between the SNRB result (positive or negative) and the probability of having surgery may differ between the USA and the UK. We therefore performed a service evaluation of all diagnostic SNRBs conducted at Cambridge University Hospitals NHS Foundation Trust between 1 April 2009 and 1 April 2010. Patients were followed up to see if lumbar spine surgery had been performed within 1 year of the SNRB and whether or not it had been performed at the level indicated by the SNRB. A positive result was defined as moderate or substantial patient-reported pain relief post SNRB. We used data from patients receiving SNRB at a single level ($n = 69$).

Forty-four patients had a positive SNRB result and, of these, 12 (27%) went on to receive surgery at the level investigated within 1 year. Of the 19 patients with a negative SNRB result, one patient (5%) went on to receive surgery at the level investigated within 1 year. The remaining six patients did not have their SNRB result recorded in the medical records although none went on to receive lumbar surgery within 1 year. In a sensitivity analysis (sensitivity analysis C) we used a threshold analysis to determine how large the therapeutic impact of SNRB would have to be in order for it to be cost-effective.

The initial (1-year) effectiveness of surgical and conservative therapy in patients with nerve root compression

Jacobs et al.[8] published a SR that compared surgery with conservative/non-surgical care in the management of sciatica in adult patients with lumbar herniated disc, consisting of five RCTs[10,11,54–56] published before October 2009. The RCTs were of variable methodological quality and heterogeneous in terms of the interventions compared (e.g. early vs delayed discectomy, discectomy vs epidural steroid injection, or discectomy vs conservative care). The narrative synthesis of the review suggested there was evidence that early surgical care is better for short-term (3-month) relief of leg pain, although only one study assessed this. Overall, the SR concluded there were no significant differences between surgery and conservative/non-operative care at 1- or 2-year follow-ups, although the evidence was scarce and interpretation was hampered in many studies because of non-compliance with surgery and crossover from conservative to surgical care.

Two of the most recent RCTs included in Jacobs et al.'s review,[8] both considered by the review authors to be at low risk of bias, also collected cost-effectiveness data. Peul et al.[9,10,12] evaluated the effects of early

lumbar surgery ($n = 141$) compared with prolonged conservative care ($n = 142$) among Dutch patients who had sciatica for between 6 and 12 weeks. Early surgery consisted of operative treatment within 2 weeks of diagnosis by experienced surgeons, while prolonged conservative care comprised 6 months of non-surgical care administered by a family practitioner. After 6 months, surgical care was allowed in the conservative care arm if it was considered necessary. Over a 2-year follow-up, the study found no difference in the scores between the two treatment arms in the Roland–Morris Disability Index[57] ($p = 0.25$), but did find a difference in leg pain which favoured early surgery ($p = 0.05$) at the 8- and 26-week follow-ups, although the differences between treatment groups diminished and were similar at 1 and 2 years post randomisation.

van den Hout et al.[12] evaluated the economic outcomes alongside the Peul et al. trial.[9,10] The study found that early surgery resulted in higher utility scores (European Quality of Life-5 Dimensions; EQ-5D) during the first 6 months. By 12 months the difference in QALYs between the surgery arm (0.78 QALYs) and prolonged conservative care arm (0.73 QALYs) was 0.044 (95% CI 0.005 to 0.083). This study may provide conservative estimates of the incremental QALYs of surgical care, as not all patients randomised to surgery received it (11% did not) and a proportion of patients randomised to prolonged conservative care (approximately 30%) received surgery within 6 months of randomisation. However, as this was a recent RCT, with a low risk of bias, conducted in a European health-care system, we used it as the primary source of data on QALY gains in our model (see Table 9).

A second RCT, the Spine Patient Outcomes Research Trial (SPORT), compared surgical with conservative management of sciatica due to LDH.[11,58,59] The SPORT LDH trial involved 501 patients with imaging-confirmed LDH and radiculopathy symptoms for at least 6 weeks. Patients were randomised either to surgery ($n = 245$) or to non-operative care ($n = 256$); a further 743 patients declined randomisation and were entered into an observational cohort. Secondary outcome measures included the EQ-5D and resource utilisation.[58] Non-adherence with randomisation was problematic, with only 59% of those randomised to surgery having received surgery by 1 year compared with 43% in the non-operative group.

The SPORT LDH economic evaluation has been reported on only an 'as treated' analysis of costs and outcomes in the randomised ($n = 501$) and observational ($n = 743$) cohorts combined and is therefore potentially affected by selection bias.[58] Of the combined cohort of patients ($n = 1191$), 775 patients received surgery at some point during the 2-year follow-up period. After adjusting for numerous baseline covariates, these patients were estimated to have mean discounted QALYs of 1.64 (95% CI 1.62 to 1.67) compared with 1.44 (95% CI 1.41 to 1.47) in patients ($n = 416$) treated non-surgically, a difference of 0.21 (95% CI 0.16 to 0.25). We used the relative differences between 1-year estimate of QALYs gained from surgery in the SPORT trial in a sensitivity analysis (sensitivity analysis D).

The initial (1-year) effectiveness of surgical and conservative therapy in patients without nerve root compression

The outcomes for patients whose symptoms were not related to the nerve root investigated by SNRB are difficult to estimate as these patients may have a wide range of causes for their symptoms. As most low back pain and referred symptoms in the lower limbs are self-limiting,[60] we assumed that outcomes in these patients would be the same as in patients with nerve root symptoms treated conservatively and that decompression surgery would not improve the prognosis (see Table 9).

If decompression surgery is performed on a patient without nerve root compression, this will have a cost to the health service and a detrimental effect on health (at least in the short term). Post-surgery patients in the van den Hout et al.[12] study experienced lower quality of life between baseline and 2 weeks (utility score 0.425 vs 0.471). We assumed that patients without nerve root compression who had surgery would have this perisurgical dip in quality of life and then recover, and have outcomes identical to patients without nerve root compression treated conservatively. This dip in quality of life was equivalent to a reduction of 0.0017 QALYs over the first year of the model (see Table 9).

TABLE 9 Variables for the diagnostic cost-effectiveness model

Variable (variable name)	Point estimate	Lower bound[a]	Upper bound[a]	Source of information	PSA distribution
Prevalence					
True nerve compression	50%	25%	75%	Clinical Opinion	Discrete estimates (0.25, 0.5, 0.75)[b]
Sensitivity/specificity					
Sensitivity SNRB	93.3%	87.3%	96.5%	Accompanying SR	Beta(112.86, 9.12)
Specificity SNRB	25.6%	5.4%	61.4%	Accompanying SR	Beta(2.35, 5.88)
Probability surgery					
No SNRB	18%			Sasso[40]	Interdependent
SNRB positive	21%	17.9%	25.6%	Sasso[40]	Beta(94, 341)
SNRB negative	8%	4.5%	13.5%	Sasso[40]	Beta(12, 130)
Probability repeat SNRB					
Equivocal SNRB leading to repeat	1.0%	0.5%	2.3%	Sasso[40]	Beta(7, 568)
Confirmation SNRB following positive result	1.9%	1.0%	3.8%	Sasso[40]	Beta(9, 404)
QALYs during the first year after treatment					
Surgery – in TPs/FNs	0.78	0.56	1	van den Hout[12]	Log-normal (0.78, 0.17)
Surgery – in FPs/TNs	0.72	0.52	1	van den Hout[12]	Log-normal (0.72, 0.17)
Conservative care in TPs/FNs	0.73	0.53	1	van den Hout[12]	Log-normal (0.73, 0.16)
Conservative care in FPs/TNs	0.73	0.53	1	van den Hout[12]	Log-normal (0.73, 0.16)
Costs (£)					
SNRB	247	133	366	NHS Reference Costs[50]	Triangular(100, 400)
Surgery	3159	1932	5435	NHS Reference Costs[50]	Triangular(1500, 6000)
Non-surgical costs in the year post surgery	1514	0	8511	van den Hout[12]	Gamma(0.39, 3875)
Non-surgical costs in the year after conservative care	1785	0	9696	van den Hout[12]	Normal[a](0.42, 4237)
Societal costs (£)					
Non-surgical societal costs in the year post surgery	12,860	640	42,822	van den Hout[12]	Gamma(1.27, 10,089)
Non-surgical societal costs in the year after conservative care	14,350	1140	43,849	van den Hout[12]	Gamma(1.58, 9109)
Discount rate					
Discount rate costs	3.5%			NICE[13]	
Discount rate outcomes	3.5%			NICE[13]	

a Percentile 95% CIs used in the probabilistic sensitivity analysis, unless stated otherwise.
b Separate deterministic sensitivity analyses run for each estimate. Not varied during PSA.

The cost of the surgical procedure

We estimated the cost of lumbar decompression surgery for radiculopathy based on HRG code. HRG codes group together spells of inpatient care for similar patients that have similar resource implications. The HRG code assigned is based on a number of variables including the primary diagnosis, major procedures performed during the admission, complications, comorbidity and length of stay. Using hospital episode statistics data for 2008–9, we ascertained the frequency with which specific HRG codes were assigned to patients who had surgery to treat lumbar nerve compression. We identified patients whose primary procedure indicated an excision of a lumbar intervertebral disc with or without laminectomy (*Table 10*). HRG code R02 (Surgery for Prolapsed Intervertebral Disc) was most commonly used, accounting for >90% of the inpatient spells (see *Table 10*). Therefore, we used the elective spell tariff (£3159) for HRG code R02 as the estimate for the initial cost of surgery (see *Table 9*).[50]

Initial non-surgical costs of care in patients with nerve root compression

The medical and societal costs during the first year following surgical and conservative care in patients with nerve root compression were taken from van den Hout *et al*.[12] Patients completed resource-use diaries to record admissions to hospital, medical visits, home help, domestic help (both professional and unpaid), drugs, other medical aids, absenteeism from work and out-of-pocket costs. van den Hout *et al*. estimated that the annual non-surgical health-care costs were €2021 (£1785) and €1714 (£1514) for prolonged conservative care and early surgical care, respectively. Societal costs in the first year, excluding the initial surgical costs, were estimated by van den Hout *et al*.[12] to be €16,270 (£14,350) and €14,581 (£12,860), respectively.

Initial non-surgical costs of care in patients without nerve root compression

We assumed that during the first year after surgical or conservative therapy, individuals with no nerve root compression would incur non-surgical costs identical to those incurred by patients with nerve root compression who had prolonged conservative care in the van den Hout *et al.* trial.[12]

The long-term costs of care

The costs (health service, social service and productivity costs) observed during the first year of the van den Hout *et al.* trial[12] were extrapolated over 20 years. The quarterly costs of care reported by van den Hout *et al*.[12] declined rapidly in both the surgical and prolonged conservative care groups over the 1-year follow-up period, although the rate of decline decreased over time (*Table 11*). In our primary extrapolation (convergence), we assumed that the average decline in quarterly costs observed in the last two quarters of the first year continued thereafter. Effectively, this assumption means that the costs of care in the surgery and prolonged conservative care arms of the trial converge after approximately 6 years.

As a secondary extrapolation (parallel – sensitivity analysis E), we assumed that the costs observed in the final quarter of the first year would be constant in all subsequent quarters for 20 years. Effectively, this assumption locks in differences in costs observed in the final quarter of the trial and represents the most optimistic assumption for cost savings achieved by correctly selecting surgical decompression in a patient with nerve root compromise (*Table 12*).

Malpractice litigation may substantially increase the long-term costs of surgery. However, recent evidence suggests that in the 9-year period from 2002 to 2010 there were just 13 cases of successful litigation against the NHS for 'wrong level'-, 'incorrect diagnosis'- or 'on-going pain'-related elective spinal surgery (which is <1 in 11,000 procedures).[61] We estimated the potential impact of litigation on the cost of surgery performed without SNRB assuming total damages and legal costs of £250,000 per successful claim in sensitivity analyses (sensitivity analysis F).

TABLE 10 Cost of surgery: frequency of HRG codes associated with OPCS codes 2008–9

OPCS 4.4 procedure code	Procedure description	HRG 3.5 code	Frequency	HRG name	% total
V331	Primary laminectomy excision of lumbar intervertebral disc	R02	1271	Surgery for prolapsed intervertebral disc	86.8
V331		R03	128	Decompression and effusion for degenerative spinal disorders	8.7
V331		Other	65	Intracranial procedures except trauma – category 3	4.4
V332	Primary fenestration excision of lumbar intervertebral disc	R02	1084	Surgery for prolapsed intervertebral disc	88.3
V332		R03	97	Decompression and effusion for degenerative spinal disorders	7.9
V332		Other	46	Intracranial procedures except trauma – category 3	3.7
V337	Primary microdiscectomy of lumbar intervertebral disc	R02	4252	Surgery for prolapsed intervertebral disc	94.7
V337		R03	155	Decompression and effusion for degenerative spinal disorders	3.5
V337		Other	85	Intracranial Procedures Except Trauma – category 2	1.9

TABLE 11 Extrapolation of cost and QALYs – assuming convergence

Year	Conservative			Surgery			
	NHS + PSS costs (£)	Societal costs (£)	Utility	NHS + PSS costs (£)	Societal costs (£)	Utility	Probability of death
0.25[a]	838	6826	0.68	862	7659	0.77	N/A
0.5[a]	409	4063	0.80	302	2529	0.83	N/A
0.75[a]	322	2422	0.81	201	1555	0.82	N/A
1[a]	210	1402	0.83	141	1087	0.86	N/A
2	396	1758	0.86	238	1693	0.88	0.001
3	106	209	0.88	52	315	0.89	0.002
4	29	25	0.89	11	59	0.89	0.002
5	8	3	0.89	2	11	0.89	0.002
6	2	0	0.89	1	2	0.89	0.002
7[b]	1	0	0.89	0	0	0.89	0.002
Total costs and QALYs (years 2–20)	541	1996	16.86	304	2081	16.89	0.074

N/A, not applicable.

a Values from van den Hout et al.[12]

b Costs and QALYs remain constant for all future years.

TABLE 12 Extrapolation of cost and QALYs – assuming parallel

Year	Conservative			Surgery			Probability of death
	NHS + PSS costs (£)	Societal costs (£)	Utility	NHS + PSS costs (£)	Societal costs (£)	Utility	
0.25[a]	838	6826	0.68	862	7659	0.77	N/A
0.5[a]	409	4063	0.80	302	2529	0.83	N/A
0.75[a]	322	2422	0.81	201	1555	0.82	N/A
1[a]	210	1402	0.83	141	1087	0.86	N/A
2	841	5607	0.83	563	4347	0.86	0.001
3	841	5607	0.83	563	4347	0.86	0.002
4	841	5607	0.83	563	4347	0.86	0.002
5	841	5607	0.83	563	4347	0.86	0.002
6	841	5607	0.83	563	4347	0.86	0.002
7[b]	841	5607	0.83	563	4347	0.86	0.002
Total costs and QALYs (years 2–20)	15,984	106,540	16.33	10,701	82,597	16.85	0.074

N/A, not applicable.

a Values from van den Hout *et al*.[12]

b Costs and QALYs remain constant for all future years.

The long-term utility scores and mortality following surgical and conservative therapy

The utility values from the van den Hout *et al*. trial[12] were extrapolated over 20 years using the same extrapolation methods [converging (see *Table 11*) and parallel (see *Table 12*)] as described for cost extrapolations. The probability of death was based on lifetable survival data and was assumed to match that of the general population.[12] The age of patients at the outset of our model was assumed to be equal to the average age of patients recruited in the van den Hout trial *et al*. (42 years).[12]

Discounting

All costs and QALYs after the first year of the model have been discounted at 3.5% per annum consistent with guidance from NICE.[13]

Probabilistic sensitivity analysis

Probabilistic sensitivity analysis was carried out to estimate the overall uncertainty in the model results due to the combined uncertainty stemming from each of the parameters used to construct the model. Parameters were randomly sampled from a probability distribution assigned to each variable (see *Table 9*). The results of these analyses are presented as cost-effectiveness acceptability curves (CEACs).

In addition, five deterministic sensitivity analyses were performed as noted in the preceding paragraphs: (1) sensitivity analysis A varied the pre-test prevalence of nerve root compression to a lower 25% and a higher 75%; (2) sensitivity analysis B used high-sensitivity/low-specificity and low-sensitivity/high-specificity estimates of diagnostic accuracy; (3) sensitivity analysis C conducted threshold analyses to examine how large the therapeutic impact of SNRB would have to be in order for it to be cost-effective; (4) sensitivity analysis D based the outcomes of surgery on 'as treated' QALY results from the SPORT LDH analysis;

and (5) in sensitivity analysis E we used the parallel extrapolation to model costs and utilities after the initial year.

Partial expected value of perfect information

The model is a simplification of the reality of diagnostic testing with SNRB, based on imperfect data. This creates a possibility that the model will reach the 'wrong' conclusion favouring a technology that would be proven to be not cost-effective were more data collected. Partial expected value of perfect information (PEVPI) analysis allows a comparison of the value of potential future research projects. A research project is less valuable if it will provide evidence on a parameter that is already precisely known from existing research or a parameter that is unimportant for the conclusion of the model. We use PEVPI to look at the value of a potential diagnostic accuracy study to more precisely estimate the sensitivity and specificity of SNRB. We used 10,000 iterations and a willingness to pay per QALY of £30,000 to calculate PEVPI per patient.

Model verification and validation

The project economists and clinicians jointly reviewed the structure of the model to ensure that it reflected clinically plausible diagnostic and therapeutic transitions. We verified the internal validity of the model using extreme value analyses for every parameter to check that the results of the model were correlated with each parameter of the model in the expected direction. We double coded the model in TreeAge Pro (TreeAge Software, Inc., Williamstown, MA, USA) and Microsoft Excel 2007 (Microsoft Corporation, Redmond, WA, USA) to identify any discrepancies or miscoding in the model.

Chapter 7 Results of cost-effectiveness study

Suspected single-level nerve root compression – cost per case detected

When the pre-test prevalence of nerve root compression is 50% and patients have suspected single-level nerve root compression, adding SNRB to the diagnostic work-up results in an additional cost of £254 (*Table 13*). SNRB also leads to an increase in patients receiving a correct diagnosis to 59.5%. Adding SNRB to the diagnostic work-up has an incremental cost of £2684 per correct diagnosis although the CI is very wide.

Suspected single-level nerve root compression – cost per quality-adjusted life-year

Although SNRB does result in a lower proportion of patients incorrectly receiving surgery (17.6% vs 18.0%; *Table 14*) and does increase surgery in patients with nerve root compression (20.1% vs 18.0%; see *Table 14*), these differences are small because of the low specificity of SNRB and the high percentage of patients who do not receive surgery despite a positive SNRB result. This marginal improvement achieved by targeting surgery at those most likely to benefit from it does lead to some savings in costs because of faster recovery during the first year. However, this does not outweigh the cost of the SNRB test plus the additional cost of surgery in the higher proportion of patients who receive it after SNRB. In terms of NHS and PSS costs, the SNRB strategy is £304 per patient more expensive. The incremental gain in QALYs due to more accurate diagnosis with SNRB is very small (0.0002; see *Table 14*). Hence, the incremental cost per QALY gained of using SNRB in patients with suspected nerve root compression at a single level is very high (£1,576,000; see *Table 14*). This is well above conventional cost-effectiveness thresholds.

If societal costs are included (e.g. lost productivity because of back and leg pain), the costs associated with both diagnostic strategies increase markedly. However, the incremental cost of SNRB is relatively similar (£261; see *Table 14*) despite this broader perspective and the cost per QALY gained is still well in excess of conventional thresholds.

There is considerable uncertainty around this estimate of cost per QALY, in large part because of the broad CIs around diagnostic accuracy identified in our SR. The CEAC (*Figure 7*) indicates a low, but not negligible, probability (2.4%) that the addition of SNRB to the diagnostic work-up will be cost-effective at a cost per QALY threshold of £30,000.

TABLE 13 Single-level nerve root compression, cost per case detected

Cost/outcome measure	No SNRB	SNRB	Difference	95% CI
Cost of SNRB testing (£)	0	254	254	141 to 374
Percentage receiving correct diagnosis	50.0	59.5	9.5	−1.6 to 26.7
Incremental cost per correct diagnosis (£)			2684	780 to dominated

TABLE 14 Single-level nerve root compression, cost per QALY gained

Cost/outcome measure	No SNRB	SNRB	Difference	95% CI
Percentage receiving surgery	18.0	18.9[a]	0.87	−2.60 to 5.22
Percentage of patients with nerve root compression receiving surgery	18.0	20.1	2.11	−0.93 to 6.53
Percentage of patients without nerve root compression receiving surgery	18.0	17.6	−0.38	−5.33 to 4.67
NHS and PSS costs (£)	2824	3127	304	−119 to 558
Societal costs	18,467	18,728	261	−277 to 859
QALYs	12.6229	12.6231	0.0002	−0.0069 to 0.0071
NHS PSS cost per QALY gained (£)			1,576,007	
Societal cost per QALY gained (£)			1,356,638	

a This percentage is based on seven parameters: the pre-test prevalence, the sensitivity and specificity of SNRB, the probability of an equivocal SNRB, the probability of a confirmation SNRB being requested, and the probability of surgery given a positive or negative SNRB finding.
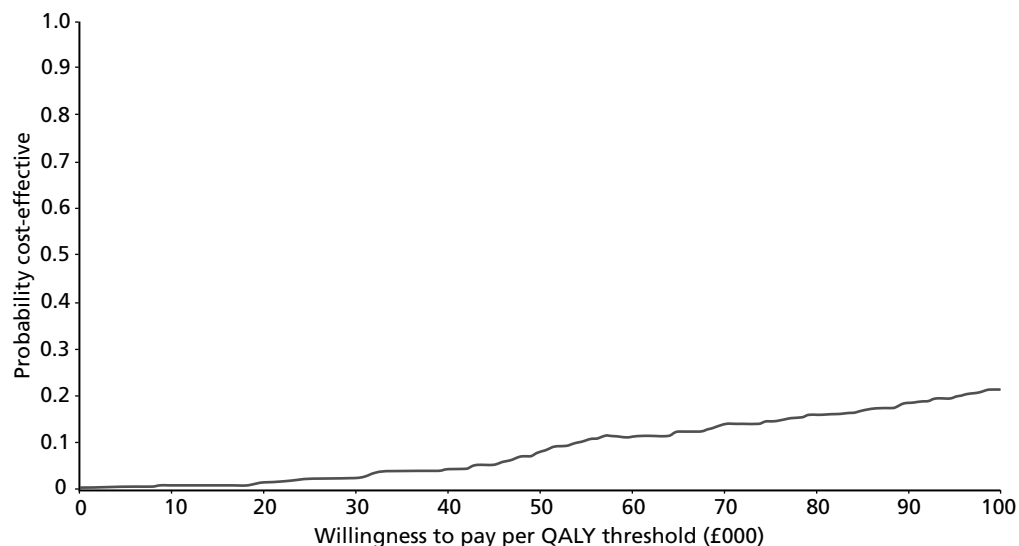
FIGURE 7 Cost-effectiveness acceptability curve – one-level nerve root compression.

Suspected two-level nerve root compression – cost per case detected

For patients with suspected two-level nerve root compression, adding SNRB to the diagnostic work-up costs £507 (*Table 15*). Compared with single-level SNRB the diagnostic accuracy is reduced, in both arms, as both levels need to be diagnosed accurately to get a correct diagnosis. As for suspected single-level compression the addition of SNRB leads to a higher proportion patients being correctly diagnosed. Adding SNRB to the diagnostic work-up has an incremental cost-effectiveness of £4903 per case correctly diagnosed. However, the CIs are again wide, reflecting the uncertainty around the diagnostic accuracy of SNRB.

Suspected two-level nerve root compression – cost per quality-adjusted life-year

The use of SNRB in patients with suspected nerve root compression at two levels was not cost-effective (*Table 16*). This was because of the increased cost of testing and the low specificity of SNRB, resulting in a large number of patients with a FP result on at least one nerve root, potentially leading to inappropriate surgery. The incremental NHS and PSS costs (£1040) were greater when SNRB was used for suspected two-level nerve root compression, while the incremental QALYs gained were negative (–0.0002). Hence, SNRB was dominated (more costly, less effective) by no additional testing in patients with suspected two-level nerve root compression.

Deterministic sensitivity analyses

There were a number of structural uncertainties and variance in patient characteristics that we chose to explore through deterministic sensitivity analysis. These sensitivity analyses were conducted on the single-level nerve root compromise model and are listed below.

(a) Sensitivity analysis about the pre-test prevalence of nerve root compression.
(b) Sensitivity analysis about the possible values of sensitivity and specificity of SNRB.
(c) Threshold sensitivity analyses to examine how large the therapeutic impact of SNRB would have to be in order for it to be cost-effective.

TABLE 15 Two-level nerve root compression, cost per case detected

Cost/outcome measure	No SNRB	SNRB	Difference	95% CI
Cost of SNRB testing (£)	0	507	507	280 to 763
Percentage receiving correct diagnosis	25.0	35.3	10.3	–1.3 to 10.9
Incremental cost per correct diagnosis (£)			4903	1264 to dominated

TABLE 16 Base-case results two level case

Cost/outcome measure	No SNRB	SNRB	Difference	95% CI
Percentage receiving surgery	18.0	20.7[a]	2.7	–3.70 to 2.57
NHS and PSS costs (£)	2838	3878	1040	545 to 1923
QALYs	12.6268	12.6265	–0.0002	–0.0825 to 0.0774
NHS PSS cost per QALY gained			Dominated	

a This percentage is based on eight parameters: the pre-test prevalence at each level, the sensitivity and specificity of SNRB, the probability of an equivocal SNRB, the probability of a confirmation SNRB being requested, and the probability of surgery given positive or negative SNRB findings.

(d) Sensitivity analysis about the maximum benefit of surgery based on 'as treated' rather than 'intention to treat' estimates.
(e) Sensitivity analysis about the extrapolation of costs and outcomes beyond 1 year.
(f) Sensitivity analysis including malpractice litigation.

Pre-test prevalence

As the prevalence of nerve root compression increases, both the incremental costs and the incremental QALYs gained by SNRB increase (*Table 17*). In a patient group with high prevalence, a test such as SNRB, which has high sensitivity but low specificity, makes more correct diagnoses and more patients appropriately receive surgery. SNRB becomes more cost-effective as prevalence increases, but even at a prevalence of 75% the incremental cost-effectiveness ratio (ICER) (£552,734) is not efficient compared with conventional thresholds of cost-effectiveness. Our conclusions are relatively insensitive to the pre-test prevalence of nerve root compression.

Sensitivity and specificity of selective nerve root block

Replacing the pooled estimate of sensitivity and specificity with data from two diagnostic accuracy studies in our SR towards the extremes of the receiver operating characteristic space (see *Figure 3*) did not change our conclusion that SNRB is unlikely to be cost-effective (*Table 18*) as increases in diagnostic accuracy are tempered by the moderate impact of the SNRB result on the decision to perform surgery.

The therapeutic impact of selective nerve root block

At a willingness to pay per QALY of £30,000 there is no probability of surgery that would lead to SNRB being cost-effective keeping all other variables constant. Even if all patients with positive SNRB results had surgery and no patients with negative SNRB results received surgery, the ICER (£87,023) is still above conventional thresholds defining cost-effectiveness.

Benefit of surgery in the first year

Using the relative difference in QALYs between surgery and conservative care from the 'as treated' group in the SPORT LDH trial and keeping our QALY gained from surgery estimate constant, the cost-effectiveness of SNRB increases with an ICER of £236,778 per QALY (*Table 19*).

Extrapolation of costs and outcomes beyond 1 year

Extrapolating the results out over 20 years using a parallel rather than a converging extrapolation assumption increases the cost-effectiveness of SNRB because the value of correctly selecting surgery in a patient with nerve root compression is increased. SNRB remains more expensive and, from the NHS and PSS perspective, the ICER remains above conventional thresholds defining efficiency (*Table 20*). However, from a societal perspective, the extra costs of SNRB are justified by the benefits of surgery and the NHS and productivity savings associated with performing surgery in those likely to benefit most. The interpretation of the model is relatively sensitive to assumptions about the long-term costs and benefits of surgery vis à vis conservative care.

Malpractice litigation

The net impact of including malpractice litigation costs on our model findings was negligible. The NHS and societal incremental cost per QALY gained still exceeded £1M.

Partial expected value of perfect information

For all values of sensitivity and specificity, holding all other variables constant, the conclusion that SNRB is not cost-effective does not change. This indicates that without further research into other variables there would be little value to undertaking further research on the diagnostic accuracy of SNRB. Even when the willingness to pay per QALY is increased to £200,000, research around the diagnostic accuracy of SNRB still has a PEVPI per patient of only £0.03, suggesting that further research would not be a high priority.

TABLE 17 Sensitivity analysis of pre-test prevalence of nerve root compression

Cost/outcome measure	25%		75%	
	No SNRB	SNRB	No SNRB	SNRB
NHS and PSS costs (£)	2846	3132	2801	3122
Societal costs (£)	18,543	18,793	18,391	18,633
QALYs	12.6189	12.6188	12.6268	12.6273
NHS PSS cost per QALY gained (£)	Dominated		552,734	
Societal cost per QALY gained (£)	Dominated		460,579	

TABLE 18 Sensitivity analysis of possible values of sensitivity and specificity of SNRB

Cost/outcome measure	Yeom et al.[38] (sensitivity 57%, specificity 86%)		Sasso et al.[40] (sensitivity 96%, specificity 56%)	
	No SNRB	SNRB	No SNRB	SNRB
NHS and PSS costs (£)	2824	2938	2824	3070
Societal costs (£)	18,467	18,567	18,467	18,669
QALYs	12.6229	12.6217	12.6229	12.6234
NHS PSS cost per QALY gained (£)	Dominated		471,171	
Societal cost per QALY gained (£)	Dominated		386,317	

TABLE 19 Sensitivity analysis using 'as-treated' values from SPORT LDH trial

Cost/outcome measure	As treated	
	No SNRB	SNRB
NHS and PSS costs (£)	2824	3127
Societal costs (£)	18,467	18,728
QALYs	12.5300	12.5312
NHS PSS cost per QALY gained (£)	236,778	
Societal cost per QALY gained (£)	203,820	

TABLE 20 Extrapolation of the costs and outcomes of surgery

Cost/outcome measure	Parallel	
	No SNRB	SNRB
NHS and PSS costs (£)	13,252	13,518
Societal costs (£)	90,063	90,138
QALYs	11.9192	11.9230
NHS PSS cost per QALY gained (£)	68,481	
Societal cost per QALY gained (£)	19,862	

Chapter 8 Discussion

Statement of principal findings

There were few studies that estimated the diagnostic accuracy of SNRB in patients with low back pain and radiculopathy in whom clinical and imaging findings are discordant or equivocal. Research on this topic is hampered by the lack of a diagnostic gold standard against which to compare tests such as SNRB. We identified five diagnostic accuracy studies,[28,38–41] all at high risk of bias. Of particular concern was the fact that many studies were at risk of verification bias, as patients with a positive SNRB were more likely to undergo surgery (the reference standard) than those testing negative. There was substantial variation in estimates of sensitivity and specificity across studies: sensitivity ranged from 57% to 100% and specificity from 10% to 86%. Based on the two cohort studies[40,41] that used post-surgery outcomes as the reference standard, the summary sensitivity was 93.3% (95% CI 85.8% to 97.0%) and summary specificity was 25.6% (95% CI 5.4% to 67.5%). However, conclusions based on these data should be tempered because of the large CIs around specificity and the high risk of bias which affects these studies.

Despite case reports[26,51,52] of serious adverse events associated with SNRB, our SR confirmed that these were very rare events. Of the seven studies[25,28,42–46] ($n > 1500$ patients) identified that reported on complications and adverse events of SNRB, no serious adverse events were reported. The largest case series[25] ($n = 1203$ adult patients) reported minor and transient complications in 5.5% of patient visits, but no major or permanent complications.

Our economic model indicated that, in the case of patients with suspected single-level nerve root compression, SNRB does increase the proportion of patients in whom presence or absence of nerve root compression (59.5% vs 50%) is accurately diagnosed and the proportion of patients with nerve root compression who undergo surgery (20.1% vs 18%). However, these benefits do not appear to be justified by the additional costs of testing. The incremental cost per additional case accurately diagnosed was £2684 and the incremental cost per QALY gained was £1,576,007. In comparison with other health interventions, reviewed by NICE on behalf of the NHS, this does not represent good value for money. This conclusion was the same for patients with suspected two-level nerve root compromise and was not altered in sensitivity analyses varying several key assumptions of the model, including prevalence, the diagnostic accuracy of SNRB, and the impact of the SNRB result on the probability of performing surgery. The model was sensitive to assumptions about the benefits of surgery beyond the 1-year follow-up reported in RCTs examining cost-effectiveness. If the residual improvement in quality-of-life (utility) scores and the savings in costs observed in the surgical arm of trials at 12 months post randomisation continues, rather than diminishes over time, then SNRB has the potential to be cost-effective, despite low specificity. However, we conclude that it is very unlikely based on the current evidence that SNRB is a cost-effective method for informing the decision to operate in patients with low back and leg pain where there is doubt about the localisation of the lesion.

Strengths and limitations of the assessment

We conducted systematic and extensive literature searches in order to locate all relevant studies that met inclusion criteria. These included electronic searches in a wide variety of databases, scanning the references of included studies and previous SRs. Diagnostic accuracy studies are very difficult to identify from electronic databases as there are no specific indexing terms. Therefore, very sensitive searches were carried out to ensure that relevant studies were not missed. Previous work has shown that inclusion of methodological search filters in searches for diagnostic accuracy studies misses relevant studies;[36] for this reason we did not use a search filter. Attempts were also made to identify unpublished studies. This

included searching conference proceedings and grey literature. It is unlikely that any relevant published studies have been missed, although it is possible that some unpublished studies were not identified.

We used a validated tool (QUADAS-2) to assess the risk of bias and applicability to the research question of the diagnostic studies included in our review. This revealed the flaws in the primary evidence on this research topic. In particular, it highlighted the verification bias inherent in the diagnostic cohort studies, in which patients with a positive SNRB result were more likely to go on to receive surgery. It also raised concerns about the within-patient case–control studies, in which patient selection was limited to patients with clear-cut clinical and imaging findings of nerve root compression. It is unclear whether or not the diagnostic accuracy results from these studies are relevant to clinical practice, in which patients in whom clinical and imaging findings are discordant are most likely to undergo SNRB. The presence of these concerns about the risk of bias and applicability of the primary data led us to interpret the primary and pooled diagnostic accuracy data cautiously.

We have extended the diagnostic accuracy review to model the costs and effects of lumbar SNRB through its impact on treatment choices and patient outcomes. This enabled us to place the evidence on the value of SNRB in a broader context and compare it with other health interventions competing for NHS resources. However, given the scarcity of high-quality primary data, the assessment of the cost-effectiveness was inevitably speculative. The uncertainty within the economic model was high and driven primarily by (a) the uncertainty surrounding the point estimates of sensitivity and specificity; (b) the lack of information on the extent to which the SNRB results influence the subsequent choice of surgical and conservative care; and (c) the limited evidence from RCTs (with substantial non-compliance with assigned therapy) about the costs and benefits of surgery in appropriately selected patients. Despite this inherent uncertainty, we were able to conclude that it is very unlikely based on the current evidence that SNRB is a cost-effective method for informing the decision to operate in patients with low back pain and radiculopathy where there is doubt about the localisation of the lesion.

Comparison with other studies

Two previous SRs of the diagnostic utility of SNRB in patients whose pain was of spinal origin have been reported.[62,63] The first used a computerised search of MEDLINE, Cumulative Index to Nursing and Allied Health Literature (CINAHL), EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) databases, while the second (an update of the first) additionally searched BioMed, abstracts from scientific meetings and screened the reference lists of included studies.

The original review by Everett *et al.*[63] included 11 diagnostic studies and the updated review by Datta *et al.*[62] included 16 diagnostic studies (*Table 21*). Both reviews provided a narrative summary of the evidence. The original review concluded that the 'available literature is supportive of selective nerve root injections as a diagnostic test in equivocal radicular pain' while calling for additional research on the topic.[63] The updated review also acknowledged the need for further research and concluded that there was 'moderate evidence for SNRBs in the preoperative evaluation of patients with negative or inconclusive imaging studies, but with clinical findings of nerve root irritation'.[62] Based on our review of the evidence, we believe that these conclusions are too strong. We found limited evidence of low methodological quality indicating that the diagnostic accuracy of SNRB is uncertain and that specificity in particular may be low.

The differences in interpretation between our review and those conducted previously may be partly due to the smaller number of primary studies included in our review. We used rigorous eligibility criteria, restricting analysis to studies that provided sufficient data to construct estimates of sensitivity and specificity. Unlike previous reviews, we restricted our analysis to studies evaluating lumbar SNRB, and therefore studies of patients with cervical spine radiculopathy were excluded. Of the five studies[28,38–41] included in our review, three[28,39,41] were also included in the updated Datta *et al.* review.[62] Of the remaining 13 included in the Datta *et al.* review[62] but excluded from our study, three studies[64–66] were

excluded as they focused on cervical spine injections (see *Table 21*). Six studies[27,67–71] were excluded from our review because it was impossible to reconstruct sensitivity and specificity or 2 × 2 tables of index test and reference standard results. Three studies[46,72,73] did not include a reference standard and were not considered diagnostic accuracy studies. In the final study,[74] it was not possible to separate results for patients with malignant and non-malignant pathology.

Datta *et al.*[62] used an earlier version of QUADAS[75] to assess the methodological quality of studies. The proportion of studies fulfilling each QUADAS item and a profile of individual studies' score on each item are not provided. Instead a combined summary score out of 14 is presented for each study, which has been shown to be an inappropriate way of summarising the results of the QUADAS assessment.[76] However, Datta *et al.*[62] state that methodological quality of the primary studies included in their review is a limitation. We agree with this assessment and acknowledge that the same limitation applies to our review.

TABLE 21 Studies included in previous published SRs and their eligibility in our review

| Author (year) | Included in other reviews | | |
	Datta[62] (2007)	Everett[63] (2005)	
Included in our review			
Dooley[41] (1988)	✓	✓	
North[39] (1996)	✓	✓	
Sasso[40] (2005)	✗	✗	
Schutz[28] (1973)	✓	✗	
Yeom[38] (2008)	✗	✗	
Excluded from our review			*Reason for exclusion from our review*
Anderberg[65] (2006)	✓	✓	Cervical SNRB
Anderberg[64] (2004)	✓	✗	Cervical SNRB
Slipman[66] (1998)	✓	✓	Cervical SNRB
Haueisen[67] (1985)	✓	✓	Only positive SNRBs received surgery reference standard. Cannot get 2 × 2
Krempen[27] (1974)	✓	✓	Only positive SNRBs received surgery reference standard. Cannot get 2 × 2
Stanley[69] (1990)	✓	✓	Only positive SNRBs received surgery reference standard. Cannot get 2 × 2
Herron[68] (1989)	✓	✓	Cannot get 2 × 2
Wolff[70] (2001)	✓	✗	Diagnostic block, but no diagnostic data reported. Cannot get 2 × 2
Wolff[71] (2006)	✓	✓	No 2 × 2 or accuracy measure. Only reports means
Faraj[72] (2006)	✓	✗	No reference standard. Testing SNRB with and without a stimulator
Tajima[46] (1980)	✓	✓	No reference standard
van Akkerveeken[74] (1993)	✓	✓	Cannot separate out the group of patients of interest from those with cancer
Wolff[73] (2006)	✗	✗	Examining epidural spread of anaesthetic, not a diagnostic study

✗, no; ✓, yes.

Unanswered questions and future research

Our review highlights the uncertain value of SNRBs when used for diagnostic purposes to establish whether or not clinical symptoms result from a particular nerve root. However, the distinction between diagnostic and therapeutic SNRBs is often not straightforward. Many centres combine local anaesthetic and periradicular steroid injections in order to gain both diagnostic information and, potentially, longer-term pain relief for the patient. Evidence collated in SRs[31,77] confirms that transforaminal epidural steroid injections can be a clinically effective and cost-effective part of a management strategy for patients with radicular pain.

Better evidence is needed to inform practice in centres that currently rely on SNRB for diagnostic information to help decide whether, or at which level, to perform lumbar decompressive surgery. These centres could perform SNRB procedures as part of research projects to improve the evidence base. Our recommendations for future research are as follows.

1. A large rigorous diagnostic cohort study to determine the diagnostic accuracy of SNRB in predicting the short-term outcome of lumbar surgery in patients with suspected radiculopathy but equivocal or discordant clinical and radiological findings.

In order to minimise bias, the SNRB result would not be made available to the surgical team and all patients would receive surgery soon after the SNRB. All SNRB results would be recorded based on a pre-specified threshold of pain reduction at fixed intervals post procedure. Similarly the outcomes of surgery (the reference standard) would be collected at a uniform period (e.g. 8 weeks) post surgery.

The research team would have to convince patients, clinicians and an ethics committee that it was acceptable to withhold potentially diagnostic SNRB information in this way, but given the poor-quality evidence on the diagnostic utility of SNRB identified by our review, this should be possible.

2. Separate or nested diagnostic cohort studies to identify the optimal SNRB technique.

In particular, lower anaesthetic volume, the use of needle provocation and the use of control injections at adjacent sites all have the potential to increase the specificity of SNRB. The variation in these parameters observed in the studies identified by our review demonstrates the lack of agreement on the optimal SNRB technique.

The diagnostic cohort studies described above would answer the question of whether or not SNRB can predict which patients will have good outcomes after surgery, which is an important first priority in demonstrating diagnostic accuracy. However, it leaves a key question unanswered, namely 'Can SNRB predict which patients will have better outcomes after surgery than if they were treated conservatively?'

3. A RCT to measure the impact of diagnostic SNRB on treatment decisions and the costs and outcomes of care for (subgroups of) patients with discordant or equivocal clinical and imaging findings of nerve root compression.

Patients would be randomised to receive either SNRB or management based on clinical and imaging findings alone. As the number of diagnostic SNRBs conducted at any one hospital is likely to be relatively small, this would need to be a multicentre trial. Even so, it may be difficult to demonstrate a difference in patient outcomes as SNRB will alter eventual management in only a subgroup of patients in whom it is performed. It may, however, be possible to provide convincing evidence on the cost-effectiveness of diagnostic SNRB if, for instance, SNRB substantially reduces the number of patients who have surgery. Researchers might choose to focus patient recruitment to this RCT on subgroups of patients, for example those with symptoms indicating potential multiple nerve root involvement, in whom SNRB is believed to be most valuable.

Chapter 9 Conclusions

Despite being widely used for many decades as a method of confirming the source of radicular pain prior to lumbar decompressive surgery, there are few studies of the diagnostic accuracy of SNRB. Based on current weak evidence it is unlikely that SNRB is a cost-effective method for determining which patients will benefit from lumbar surgery.

Better diagnostic accuracy studies are needed to determine whether or not the use of SNRB in the diagnostic work-up of patients with discordant clinical and imaging findings of nerve root compression can identify patients who will have good outcomes after surgery. A trial randomising patients to treatment based on clinical and imaging findings alone or treatment based on these findings plus SNRB is needed to establish whether or not diagnostic SNRB can improve the process and outcomes of care.

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Contribution of authors

Rebecca Beynon (Research Associate, Health Services Research) conducted the reviews of diagnostic accuracy and adverse events, conducted analyses and completed the first draft of the report.

James Hawkins (Research Assistant, Health Economics) developed the economic model, analysed the model findings, conducted value of information analysis and drafted *Chapter 6* and *7*.

Rodney Laing (Consultant Neurosurgeon) contributed to the conception and design of the study, provided clinical expertise in neurosurgery, helped with acquisition of data for the service evaluation of SNRB and critically revised the draft report.

Nicholas Higgins (Consultant Radiologist) contributed to the conception and design of the study, provided clinical expertise in neuroradiology, helped with acquisition of data for the service evaluation of SNRB and critically revised the draft report.

Penny Whiting (Senior Research Fellow, Health Services Research) contributed to the conception and design of the study, supervised conduct of reviews of diagnostic accuracy and adverse events, and critically revised the draft report.

Catherine Jameson (Research Associate, Health Services Research) conducted the reviews of diagnostic accuracy and adverse events.

Jonathan Sterne (Professor, Medical Statistics and Epidemiology) contributed to the conception and design of the study, supervised conduct of the meta-analysis and critically revised the draft report.

Pierluigi Vergara (Clinical fellow in neurosurgery) led on the acquisition of data for the service evaluation of SNRB and critically revised the draft report.

William Hollingworth (Reader, Health Economics) was principal investigator on the project, contributed to the conception and design of the study, supervised conduct of reviews of diagnostic accuracy and adverse events, supervised construction of the economic model and critically revised the draft report.

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Appendix 1　Literature search strategies

All searches carried out from inception of database to 21 October 2010.

Database: MEDLINE 1950 to present

Search strategy

1. exp Back Pain/
2. back pain.tw.
3. backache.tw.
4. Radiculopathy/
5. Lumbar Vertebrae/
6. Lumbosacral Region/
7. radiculopath$.tw.
8. lumbago.tw.
9. lumber.tw.
10. lumbosacral.tw.
11. radiculitis.tw.
12. (radicular adj3 pain).tw.
13. spinal pain.tw.
14. exp Spinal Nerve Roots/
15. Sciatica/
16. lumbar.tw.
17. sciatica.tw.
18. Intervertebral Disk Displacement/
19. Zygapophyseal Joint/
20. Spinal Stenosis/
21. Foraminal Stenosis.tw.
22. Foramenal Stenosis.tw.
23. lateral recess stenosis.tw.
24. or/1-23
25. exp Nerve Block/
26. (nerve adj3 block$).tw.
27. SNRB.tw.
28. (transforaminal adj3 injection$).tw.
29. Injections, Epidural/
30. (neural adj3 block$).tw.
31. (nerve adj3 injection$).tw.
32. (nerve adj3 infiltration).tw.
33. (block adj3 anesthetic$).tw.
34. exp Injections, Spinal/
35. facet block$.tw.
36. facet injection$.tw.
37. epidural injection$.tw.
38. Injections, Intra-Articular/
39. diagnostic injection$.tw.
40. or/25-39
41. 24 and 40
42. exp Anesthetics, Local/

43. lidocaine.tw.
44. lignocaine.tw.
45. local an?esthetic$.tw.
46. bupivacaine.tw.
47. exp Triamcinolone/
48. Triamcinolone.tw.
49. volon.tw.
50. aristocort.tw.
51. Depo-medrone.tw.
52. Depomedrone.tw.
53. Steroids/
54. Depo steroid$.tw.
55. Deposteroid$.tw.
56. kenalog.tw.
57. kenacort.tw.
58. Depo-Medrol.tw.
59. depomedrol.tw.
60. exp Betamethasone/
61. betamethasone.tw.
62. exp prednisolone/
63. prednisolone.tw.
64. methylprednisolone.tw.
65. ((steroid$ or corticosteroid$) adj5 (injection$ or infiltration or block)).tw.
66. or/42-65
67. Diagnosis/
68. diagnosis, differential/
69. diagnosis.fs.
70. diagnos$.tw.
71. or/67-70
72. 66 and 71
73. 24 and 72
74. 41 or 73
75. exp animals/ not humans/
76. 74 not 75

Database: EMBASE 1980 to 2010 week 41

Search strategy
1. exp backache/
2. back pain.tw.
3. backache.tw.
4. exp Radiculopathy/
5. Lumbar Vertebra/
6. back/
7. radiculopath$.tw.
8. lumbago.tw.
9. (lumbar or lumber).tw.
10. lumbosacral.tw.
11. radiculitis.tw.
12. (radicular adj3 pain).tw.
13. spinal pain.tw.
14. spinal root/

15. zygapophyseal joint/
16. lumbar spine/
17. discogenic pain/
18. intervertebral disk hernia/
19. ischialgia/
20. sciatica.tw.
21. Spinal Stenosis/
22. Foraminal Stenosis.tw.
23. Foramenal Stenosis.tw.
24. lateral recess stenosis.tw.
25. or/1-24
26. exp Nerve Block/
27. (nerve adj3 block$).tw.
28. SNRB.tw.
29. (transforaminal adj3 injection$).tw.
30. epidural drug administration/
31. (neural adj3 block$).tw.
32. (nerve adj3 injection$).tw.
33. (nerve adj3 infiltration).tw.
34. (block adj3 anesthetic$).tw.
35. intraspinal drug administration/
36. facet block$.tw.
37. facet injection$.tw.
38. epidural injection$.tw.
39. intraarticular drug administration/
40. diagnostic injection$.tw.
41. or/26-40
42. 25 and 41
43. exp local anesthetic agent/
44. lidocaine.tw.
45. lignocaine.tw.
46. local an?esthetic$.tw.
47. bupivacaine.tw.
48. Triamcinolone/
49. Triamcinolone.tw.
50. volon.tw.
51. aristocort.tw.
52. Depo-medrone.tw.
53. Depomedrone.tw.
54. Steroids/
55. Depo steroid$.tw.
56. Deposteroid$.tw.
57. kenalog.tw.
58. kenacort.tw.
59. Depo-Medrol.tw.
60. depomedrol.tw.
61. Betamethasone/
62. betamethasone.tw.
63. ((steroid$ or corticosteroid$) adj5 (injection$ or infiltration or block)).tw.
64. prednisolone/
65. prednisolone.tw.
66. methylprednisolone/
67. methylprednisolone.tw.

68. or/43-67
69. Diagnosis/
70. diagnostic procedure/
71. diagnostic test/
72. diagnosis, differential/ (263,601)
73. di.fs.
74. diagnos$.tw.
75. or/69-74
76. 68 and 75
77. 25 and 76
78. 42 or 77
79. (exp animals/ or nonhuman/) not humans/
80. 78 not 79

ISI Web of Knowledge

#11 #10 AND #6
#10 #9 OR #8 OR #7
#9   ts=("Foraminal Stenosis" or "Foramenal Stenosis" or "lateral recess stenosis")
#8   ts=(sciatica or Zygapophyseal or intervertebral)
#7   TS=("back pain" or backache or radiculopathy or lumbago or lumbar or lumbosacral or lumbo-sacral or radiculitis or (radicular same pain) or "spinal pain" or ("spinal nerve root*"))
#6   #5 OR #4 OR #3 OR #2 OR #1
#5   TS=((Triamcinolone or volon or aristocort or Depo-medrone or Depomedrone or Depo-steroid* or Deposteroid* or kenalog or kenacort or Depo-Medrol or depomedrol or betamethasone or Prednisolone or methlylprednisolone) and diagnos*)
#4   ts=(((steroid same injection*) or (corticosteroid same injection*) or (steroid same infiltation) or (corticosteroid same infiltration) or (steroid same block) or (corticosteroid same block)) and diagnos*)
#3   TS=(("local anaesthetic" or "local anesthetic" or lidocaine or lignocaine or bupivacaine) and (diagnos*))
#2   ts=((spinal same injection*) or (facet same block*) or (facet same injection*) or (epidural injection*) or (intra-articular same injection*) or (diagnostic same injection*) or "diagnostic block*")
#1   ts=((nerve* same block*) or SNRB or (transforaminal same injection*) or (neural same block*) or (nerve same injection*) or (nerve same infiltration) or (anaesthetic same block*) or (anesthetic same block*))

Bioscience Information Service

#13 #11 not #12
#12 TS=(animal* not human*)
#11 #10 AND #6
#10 #9 OR #8 OR #7
#9   ts=("Foraminal Stenosis" or "Foramenal Stenosis" or "lateral recess stenosis")
#8   ts=(sciatica or Zygapophyseal or intervertebral)
#7   TS=("back pain" or backache or radiculopathy or lumbago or lumbar or lumbosacral or lumbo-sacral or radiculitis or (radicular same pain) or "spinal pain" or ("spinal nerve root*"))
#6   #5 OR #4 OR #3 OR #2 OR #1
#5   TS=((Triamcinolone or volon or aristocort or Depo-medrone or Depomedrone or Depo-steroid* or Deposteroid* or kenalog or kenacort or Depo-Medrol or depomedrol or betamethasone or Prednisolone or methlylprednisolone) and diagnos*)

#4   ts=(((steroid same injection*) or (corticosteroid same injection*) or (steroid same infiltation) or (corticosteroid same infiltration) or (steroid same block) or (corticosteroid same block)) and diagnos*)

#3   TS=(("local anaesthetic" or "local anesthetic" or lidocaine or lignocaine or bupivacaine) and (diagnos*))

#2   ts=((spinal same injection*) or (facet same block*) or (facet same injection*) or (epidural injection*) or (intra-articular same injection*) or (diagnostic same injection*) or "diagnostic block*")

#1   ts=((nerve* same block*) or SNRB or (transforaminal same injection*) or (neural same block*) or (nerve same injection*) or (nerve same infiltration) or (anaesthetic same block*) or (anesthetic same block*))

Latin American and Caribbean Health Sciences Literature

((("BACKACHE$") or "LUMBAR") or "BACK") or "RADICULOPATHY" or "RADICULOPATIA/" [Words] and (("NERVE BLOCK") or ("INFILTRATION") or ("FACET BLOCK") [Words])or (("NERVE BLOCK") [Subject descriptor]))

British Library's Electronic Table of Contents

[terms automatically 'and' ed in each line; results for each line downloaded]
Back pain block
Back pain infiltration
Radiculopathy block
Radiculopathy infiltration
SNRB
Lumbar nerve block
Facet injection
Selective nerve root block
Selective nerve root infiltration
Nerve infiltration
Facet block
Transforaminal injection

Networked Digital Library of Theses and Dissertations and other theses indices

Combinations based on (Back pain, lumbar) and (transforaminal, infiltration, facet injection, SNRB, nerve block, nerve root block)

Appendix 2 Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist

Section/topic	Number	Checklist item	Reported on page number
Title			
Title	1	Identify the report as a SR, meta-analysis or both	i
Abstract			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; SR registration number	v, vi
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known	1–4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes and study design (PICOS)	5
Methods			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g. web address) and, if available, provide registration information including registration number	*Appendix 7*
Eligibility criteria	6	Specify study characteristics (e.g. PICOS, length of follow-up) and report characteristics (e.g. years considered, language, publication status) used as criteria for eligibility, giving rationale	7, 8
Information sources	7	Describe all information sources (e.g. databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated	*Appendix 1*
Study selection	9	State the process for selecting studies (i.e. screening, eligibility, included in SR and, if applicable, included in the meta-analysis)	7
Data collection process	10	Describe method of data extraction from reports (e.g. piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators	7
Data items	11	List and define all variables for which data were sought (e.g. PICOS, funding sources) and any assumptions and simplifications made	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis	8
Summary measures	13	State the principal summary measures (e.g. risk ratio, difference in means)	9
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g. I^2) for each meta-analysis	9

Section/topic	Number	Checklist item	Reported on page number
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g. publication bias, selective reporting within studies)	8
Additional analyses	16	Describe methods of additional analyses (e.g. sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified	9
Results			
Study selection	17	Give numbers of studies screened, assessed for eligibility and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram	11
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g. study size, PICOS, follow-up period) and provide the citations	12–14
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12)	14–18
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and CIs, ideally with a forest plot	19–20
Synthesis of results	21	Present results of each meta-analysis done, including CIs and measures of consistency	18
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15)	N/A
Additional analysis	23	Give results of additional analyses, if done [e.g. sensitivity or subgroup analyses, meta-regression (see Item 16)]	20
Discussion			
Summary of evidence	24	Summarise the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g. health-care providers, users and policy makers)	45
Limitations	25	Discuss limitations at study and outcome level (e.g. risk of bias) and at review level (e.g. incomplete retrieval of identified research, reporting bias)	45, 46
Conclusions	26	Provide a general interpretation of the results in the context of other evidence and implications for future research	49
Funding			
Funding	27	Describe sources of funding for the SR and other support (e.g. supply of data); role of funders for the SR	vi

N/A, not applicable.

Adapted from Moher D, Liberati A, Tetzlaff J, Altman DG, the PRISMA Group. *Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the PRISMA statement. PLoS Med* 2009;**6**:e1000097. doi:10.1371/journal.pmed1000097

For more information visit: www.prisma-statement.org.

Appendix 3 The QUADAS-2 tool for methodological assessment of diagnostic studies

Phase 1: State the review question (this has been filled in for the current review)

Patients: Patients with lower back pain and radiculopathy (or sciatica) with non-congruent imaging and clinical findings who might benefit from lumbar decompression surgery
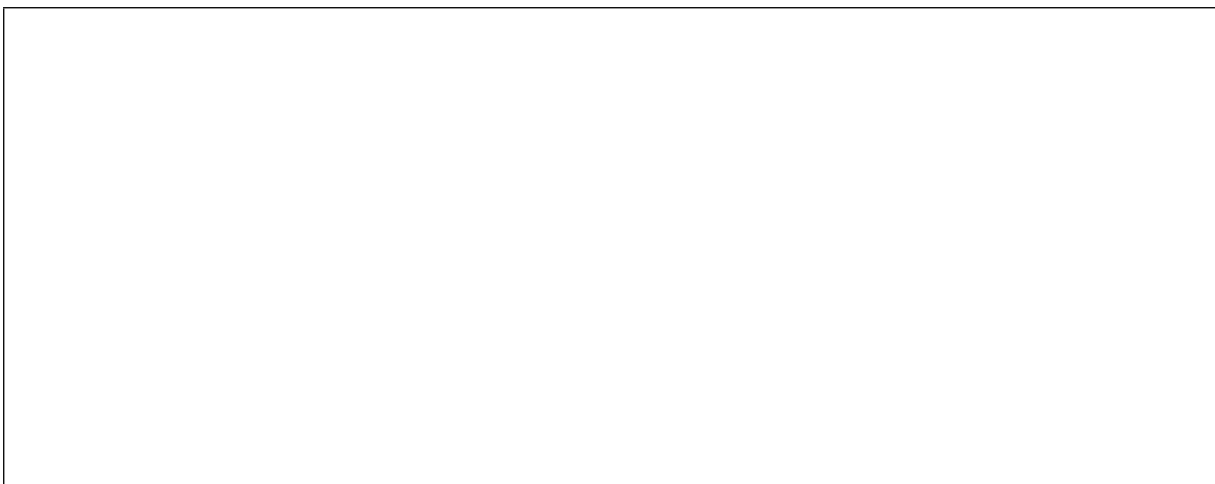
Index test: Selective Nerve Root Block including injection of anaesthetic close to the lumbar nerve root under guidance by fluoroscopy or other imaging

Target condition: Radiculopathy (or sciatica) amenable to surgery

Reference standard: Outcome following surgery

Phase 2: Draw a flow diagram for the primary study

QUADAS-2 is structured so that four key domains are each rated in terms of the risk of bias and the concern regarding applicability to the research question (as defined above). Each key domain has a set of signalling questions to help reach the judgements regarding bias and applicability. There is also an optional domain for reviews that evaluate multiple index tests which should be assessed if patients were randomised to different index tests or if individual patients received multiple index tests.

Phase 3: Risk of bias and applicability judgements

DOMAIN 1: PATIENT SELECTION

A. Risk of Bias

Describe methods of patient selection:

● Was a consecutive or random sample of patients enrolled?	Yes/No/Unclear
● Was a case-control design avoided?	Yes/No/Unclear
● Did the study avoid inappropriate exclusions?	Yes/No/Unclear
Could the selection of patients have introduced bias?	**RISK: LOW/HIGH/UNCLEAR**

B. Concerns regarding applicability

Describe included patients (prior testing, presentation, intended use of index test and setting):

Are there concerns that the included patients do not match the review question?	**CONCERN: LOW/HIGH/UNCLEAR**

DOMAIN 2: INDEX TEST(S)
If more than one index test was used, please complete for each test.

A. Risk of Bias

Describe the index test and how it was conducted and interpreted:

● Were the index test results interpreted without knowledge of the results of the reference standard?	Yes/No/Unclear
● If a threshold was used, was it pre-specified?	Yes/No/Unclear
Could the conduct or interpretation of the index test have introduced bias?	**RISK: LOW/HIGH/UNCLEAR**

B. Concerns regarding applicability

Are there concerns that the index test, its conduct, or interpretation differ from the review question?	**CONCERN: LOW/HIGH/UNCLEAR**

DOMAIN 3: REFERENCE STANDARD

A. Risk of Bias

Describe the reference standard and how it was conducted and interpreted:

● Is the reference standard likely to correctly classify the target condition?　　　Yes/No/Unclear

● Were the reference standard results interpreted without knowledge of the results of the index test?　　　Yes/No/Unclear

Could the reference standard, its conduct, or its interpretation have introduced bias?　　　**RISK: LOW/HIGH/UNCLEAR**

B. Concerns regarding applicability

Are there concerns that the target condition as defined by the reference standard does not match the review question?　　　**CONCERN: LOW/HIGH/UNCLEAR**

DOMAIN 4: FLOW AND TIMING

A. Risk of Bias

Describe any patients who did not receive the index test(s) and/or reference standard or who were excluded from the 2×2 table (refer to flow diagram):

Describe the time interval and any interventions between index test(s) and reference standard:

● Was there an appropriate interval between index test(s) and reference standard?　　　Yes/No/Unclear

● Did all patients receive a reference standard?　　　Yes/No/Unclear

● Did patients receive the same reference standard?　　　Yes/No/Unclear

● Were all patients included in the analysis?　　　Yes/No/Unclear

Could the patient flow have introduced bias?　　　**RISK: LOW/HIGH/UNCLEAR**

Appendix 4 Table of studies excluded following full paper assessment, with reasons for exclusion

First author	Publication year	Title	Reason for exclusion[a]
Abram SE	1979	Nerve blocks for low back pain	1
Ackerman WE	2008	Pain relief with intraarticular or medial branch nerve blocks in patients with positive lumbar facet joint SPECT imaging: a 12-week outcome study	2
Aguirre DA	2005	Spinal CT-guided interventional procedures for management of chronic back pain	4
Anderberg L	2004	Selective diagnostic cervical nerve root block – correlation with clinical symptoms and MRI-pathology	2
Anderberg L	2007	Transforaminal steroid injections for the treatment of cervical radiculopathy: a prospective and randomised study	2
Anderberg L	2006	Selective diagnostic nerve root block for the evaluation of radicular pain in the multilevel degenerated cervical spine	2
Anderberg L	2006	Distribution patterns of transforaminal injections in the cervical spine evaluated by multi-slice computed tomography	2
Arnhoff FN	1977	Follow-up status of patients treated with nerve blocks for low-back pain	1
Arnold PM	2009	Efficacy of injection therapy for symptomatic lumbar synovial cysts	1
Auroy Y	2002	Major complications of regional anesthesia in France: The SOS Regional Anesthesia Hotline Service	2
Auroy Y	1997	Serious complications related to regional anesthesia: results of a prospective survey in France	2
Balague F	1998	How to recognize and treat specific low back pain?	1
Ball HC	1964	Experiences with therapeutic nerve blocks	2
Bard H	1996	Lumbar nerve root infiltrations	1
Bartynski WS	2010	Adjacent double-nerve root contributions in unilateral lumbar radiculopathy	5
Bernard TN	1988	Posterior facet joint injection, selective nerve root sheath infiltration, and lumbar discography followed by computerized-tomography – refining the diagnosis in low-back pain	5
Bilinski P	1985	The lignocaine test in the diagnosis of pain in the lumbosacral spine	5
Blankenbaker DG	2005	Lumbar radiculopathy: treatment with selective lumbar nerve blocks – comparison of effectiveness of triamcinolone and betamethasone injectable suspensions	4
Bonetti M	2005	Intraforaminal O(2)–O(3) versus periradicular steroidal infiltrations in lower back pain: randomized controlled study	4
Bourne IHJ	2000	Tender point injection of corticosteroid in the treatment of backache	2
Boxem KV	2009	Re: Staal JB, de Bie R, de Vet HC, et al. Injection therapy for subacute and chronic low-back pain	1

First author	Publication year	Title	Reason for exclusion[a]
Brena SF	1990	Chronic back pain: electromyographic, motion and behavioral assessments following sympathetic nerve blocks and placebos	2
Bridenbaugh PO	1974	Role of epinephrine in regional block anesthesia with etidocaine: a double-blind study	2
Brothers MA	1968	Evaluation of low back pain by differential spinal block	3
Brull R	2007	Neurological complications after regional anesthesia: contemporary estimates of risk	1
Bundens DA	1985	Lumbar nerve root injection as an adjunct to sciatica diagnosis	6
Burgher AH	2011	Transforaminal epidural Clonidine versus corticosteroid for acute lumbosacral radiculopathy due to intervertebral disc herniation	4
Carragee EJ	2004	Diagnostic evaluation of low back pain	1
Castro WH	1991	The diagnostic value of selective lumbar nerve root block	6
Castro WH	1994	How reliable is lumbar nerve root sheath infiltration?	5
Chandler G	2000	Comparison of thoracic versus lumbar Gray Ramus communicans nerve block in the treatment of painful osteoporotic vertebral compression fracture	4
Chapman SL	1982	Learned helplessness and responses to nerve blocks in chronic low back pain patients	5
Collucci J	1992	Complications of blinded lumbar sympathetic blocks	2
Cowan NC	1992	The natural history of sciatica: a prospective radiological study	3
Crall TS	2006	The diagnostic effect of various needle tip positions in selective lumbar nerve blocks: an analysis of 1202 injections	5
Culling RD	1992	Corticosteroid injections for chronic low back pain	1
Daffner SD	2010	Cost and use of conservative management of lumbar disc herniation before surgical discectomy	2
Dam W	1974	Peripheral nerve blocks in relief of intractable pain	1
De Tran QH	2007	A review of approaches and techniques for lower extremity nerve blocks	1
Derby R	1992	Response to steroid and duration of radicular pain as predictors of surgical outcome	6
Dooley J	1986	Nerve root infiltration in the diagnosis of radicular pain	7
Fairbank J	1999	The use and interpretation of diagnostic nerve root blocks	1
Faraj AA	2006	The value of nerve root infiltration for leg pain when used with a nerve stimulator	5
Gallucci M	2007	Sciatica: treatment with intradiscal and intraforaminal injections of steroid and oxygen-ozone versus steroid only	3
Ghahreman A	2010	The efficacy of transforaminal injection of steroids for the treatment of lumbar radicular pain	3
Gharibo CG	1999	Spinal injections in diagnosis and treatment of low back pain	1
Gillies JH	1997	Corticosteroid injections for sciatica	1
Gulevich S	2009	Sciatic and suprascapular nerve block are effective for back and neck/shoulder pain	5
Haaker R	1999	Complications of injection treatment of the cervical spine and the lumbar spine	1

First author	Publication year	Title	Reason for exclusion[a]
Hanefeld C	2005	Effects of lumbar spinal nerve analgesia on the cardiovascular system	4
Hatangdi VS	1975	Management of intractable pain: the scope and role of nerve blocks: review of one year's experience	3
Haueisen DC	1985	The diagnostic accuracy of spinal nerve injection studies. Their role in the evaluation of recurrent sciatica	6
Hebl JR	2010	Neuraxial blockade in patients with pre-existing spinal stenosis, lumbar disk disease, or prior spine surgery: efficacy and neurologic complications	4
Herron LD	1989	Selective nerve root block in patient selection for lumbar surgery: surgical results	6
Hildebrandt J	2001	Relevance of nerve blocks in treating and diagnosing low back pain – is the quality decisive?	1
Huston CW	2005	Complications and side effects of cervical and lumbosacral selective nerve root injections	2
Jonsson B	1993	Symptoms and signs in degeneration of the lumbar spine. A prospective, consecutive study of 300 operated patients	3
Jonsson B	1988	Diagnostic lumbar nerve root block	6[b]
Jurg S	2009	Block of the sinuvertebral nerve: diagnostic value for lumbar discogenic pain and effect on central hypersensitivity	6
Jussila P	1976	Spinal nerve block – diagnostic test in sciatica	1
Karaman H	2011	The complications of transforaminal lumbar epidural steroid injections	4
Karnaugh RD	2010	Large lumbar disk herniations: a clinical outcome study of nonsurgical treatment	4
Karppinen J	2001	Periradicular infiltration for sciatica – a randomized controlled trial	4
Karppinen J	2001	Cost effectiveness of periradicular infiltration for sciatica: subgroup analysis of a randomized controlled trial	4
Kissin I	1989	Blockade of sciatic nerve branches relieves sciatic radicular pain	5
Krempen JF	1974	Nerve-root injection: a method for evaluating the etiology of sciatica	4
Krempen JF	1975	Selective nerve root infiltration for the evaluation of sciatica	1
Law P	2009	Can lumbar spine MRI appearances reliably predict the outcome of selective lumbar nerve root blocks?	5
Liu WJ	1983	Diagnostic and therapeutic value of nerve root infiltration in lumbago and radiculopathy	7
Liu H	2003	Characteristics of nerve root compression caused by degenerative lumbar spinal stenosis with scoliosis	4
Lynch J	1997	Transient radicular irritation after spinal anesthesia with hyperbaric 4% mepivacaine	5
Macrea LM	2009	Influencing factors on the short time outcome of diagnostic radicular blocks for sciatica	5
Manchikanti L	2007	Evaluation of lumbar facet joint nerve blocks in the management of chronic low back pain: preliminary report of a randomized, double-blind controlled trial	2

First author	Publication year	Title	Reason for exclusion[a]
Manchikanti L	2010	Making sense of the accuracy of diagnostic lumbar facet joint nerve blocks: an assessment of the implications of 50% relief, 80% relief, single block, or controlled diagnostic blocks	2
Manchikanti L	2006	The effect of sedation on diagnostic validity of facet joint nerve blocks: an evaluation to assess similarities in population with involvement in cervical and lumbar regions	3
Manchikanti L	2000	The diagnostic validity and therapeutic value of lumbar facet joint nerve blocks with or without adjuvant agents	6
Manchikanti L	2002	Periradicular infiltration for sciatica	1
Manchikanti L	2010	Evaluation of lumbar facet joint nerve blocks in managing chronic low back pain: a randomized, double-blind, controlled trial with a 2-year follow-up	2
Manchikanti L	2003	Are diagnostic lumbar medial branch blocks valid? Results of 2-year follow-up	3
Manning DC	1997	Corticosteroid injections for sciatica	1
Marks RC	1992	Facet joint injection and facet nerve block: a randomised comparison in 86 patients with chronic low back pain	4
McCollum DE	1964	The use of graduated spinal anesthesia in the differential diagnosis of pain of the back and lower extremities	3
Medel P	2007	Evaluation of functionality and pain intensity before and after a transformial steroid injection in a preliminary sample of patients with lumbar radiculopathy due to a disk hernia	3
Mendez R	2005	Evaluation of the L2 spinal nerve root infiltration as a diagnostic tool for discogenic low back pain	2
Merryman JM	2000	Diagnostic blocks of the lower back – a clinical interpretation	1
Nakamura SI	1996	The afferent pathways of discogenic low-back pain. Evaluation of L2 spinal nerve infiltration	5
Narozny M	2001	Therapeutic efficacy of selective nerve root blocks in the treatment of lumbar radicular leg pain	4
Ng LCL	2004	Outcomes of a prospective cohort study on peri-radicular infiltration for radicular pain in patients with lumbar disc herniation and spinal stenosis	4
Novak S	2008	RE: cost-effectiveness of diagnostic medial branch blocks before radiofrequency denervation	1
Nowakowski A	2007	Modified algorithm in treatment of patients with chronic low back pain with neuroradiological diagnostic techniques	5
Ochoa G	2010	Disc herniation related sciatica – radicular pain: an expression of a complex regional pain syndrome?	1
O'Neill C	1999	Precision injection techniques for diagnosis and treatment of lumbar disc disease	1
Pampati S	2009	Accuracy of diagnostic lumbar facet joint nerve blocks: a 2-year follow-up of 152 patients diagnosed with controlled diagnostic blocks	2
Pang WW	1998	Application of spinal pain mapping in the diagnosis of low back pain – analysis of 104 cases	2
Pasetto A	1981	Anesthetic block of the articular nerves of luschka in the diagnosis and treatment of lumbar and sciatic pain	2

First author	Publication year	Title	Reason for exclusion[a]
Pasetto A	1983	Epidural and spinal block in the diagnosis and treatment of lumbar and sciatic nerve pain	7
Pelz DM	1992	Percutaneous lumbar nerve root blocks	6
Petersohn JD	2004	Predicting outcomes of transforaminal injections for sciatica	1
Pfirrmann CW	2001	Selective nerve root blocks for the treatment of sciatica: evaluation of injection site and effectiveness – a study with patients and cadavers	1
Plastaras CT	2010	Inadvertent intradiscal contrast flow during lumbar transforaminal epidural steroid injections: a case series examining the prevalence of intradiscal injection as well as potential associated factors and adverse events	4
Porter DG	1999	A retrospective study to assess the results of CT-directed peri-neural root infiltration in a cohort of 56 patients with low back pain and sciatica	6
Porzelius J	1995	Memory for pain after nerve-block injections	2
Quinn SF	1988	CT-guided nerve root block and ablation	6[b]
Riew KD	2006	Nerve root blocks in the treatment of lumbar radicular pain. A minimum five-year follow-up	4
Riew KD	2000	The effect of nerve-root injections on the need for operative treatment of lumbar radicular pain. A prospective, randomized, controlled, double-blind study	4
Sato M	2009	Ultrasound and nerve stimulation-guided L5 nerve root block	6
Schliessbach J	2009	Anaesthetic block of the sinuvertebral nerve: diagnostic value for discogenic pain and modulation of central sensitisation	3
Schliessbach J	2010	Blockade of the sinuvertebral nerve for the diagnosis of lumbar diskogenic pain: an exploratory study	3
Sequeiros RB	2002	MRI-guided periradicular nerve root infiltration therapy in low-field (0.23-T) MRI system using optical instrument tracking	4
Sluijter ME	1981	Percutaneous facet denervation and partial posterior rhizotomy	3
Smith CC	2010	Interlaminar versus transforaminal epidural steroid injections for the treatment of symptomatic lumbar spinal stenosis	4
Stalcup ST	2006	Influence of needle-tip position on the incidence of immediate complications in 2,217 selective lumbar nerve root blocks	4[b]
Stallmeyer MJ	2002	Facet blocks and sacroiliac joint injections	1
Stanley D	1990	A prospective study of nerve root infiltration in the diagnosis of sciatica. A comparison with radiculography, computed tomography, and operative findings	6
Taguchi T	2002	Reassessment of the diagnostic value of selective lumbosacral radiculography	5
Tajima T	1982	Selective lumbosacral radiculography and block	5[b]
Tang S	2007	Sufentanil does not enhance the efficacy of ropivacaine in combined lumbar plexus and sciatic block: a controlled, randomised clinical trial	2
Thackeray A	2010	A pilot study examining the effectiveness of physical therapy as an adjunct to selective nerve root block in the treatment of lumbar radicular pain from disk herniation: a randomized controlled trial	4

First author	Publication year	Title	Reason for exclusion[a]
Thomas E	2001	Epidural versus foraminal corticoid injections in discal radiculopathy. A double-blind controlled trial	4
Thomas E	2003	Efficacy of transforaminal versus interspinous corticosteroid injectionin discal radiculalgia – a prospective, randomised, double-blind study	3
Tosteson ANA	2008	The cost effectiveness of surgical versus nonoperative treatment for lumbar disc herniation over two years: evidence from the Spine Patient Outcomes Research Trial (SPORT)	3
van Akkerveeken PF	1993	The diagnostic value of nerve root sheath infiltration	6
Viton JM	1998	Short-term assessment of periradicular corticosteroid injections in lumbar radiculopathy associated with disc pathology	4
Weiner BK	1997	Foraminal injection for lateral lumbar disc herniation	4
White AH	1983	Injection techniques for the diagnosis and treatment of low back pain	7
Willburger RE	2005	Side effects and complications of injection therapy for degenerative spinal disorders	4
Wilppula E	1977	Spinal nerve block. A diagnostic test in sciatica	6
Wolff AP	2001	Diagnostic lumbosacral segmental nerve blocks with local anesthetics: a prospective double-blind study on the variability and interpretation of segmental effects	5
Wolff AP	2006	Influence of needle position on lumbar segmental nerve root block selectivity	5
Wolff AP	2006	Do diagnostic segmental nerve root blocks in chronic low back pain patients with radiation to the leg lack distinct sensory effects? A preliminary study	6
Xavier AV	1988	Relief of sciatic radicular pain by sciatic nerve block	5

a Reason for exclusion: 1, not a primary study; 2, not patients with low back pain and radicular/lower limb pain; 3, not SNRB; 4, therapeutic not diagnostic; 5, not diagnostic study of SNRB; 6, unable to get 2 × 2 data; 7, unable to retrieve paper.

b Included in review of complications following diagnostic SNRB.

Note: this is a hierarchical model so although a paper could be excluded for more than one reason, the reviewer excluded a paper as soon as one criteria was not fulfilled.

Appendix 5 Studies included in the diagnostic review

1. Dooley JF, McBroom RJ, Taguchi T, Macnab I. Nerve root infiltration in the diagnosis of radicular pain. *Spine* 1988;**13**:79–83.
2. North RB, Kidd DH, Zahurak M, Piantadosi S. Specificity of diagnostic nerve blocks: a prospective, randomized study of sciatica due to lumbosacral spine disease. *Pain* 1996;**65**:77–85.
3. Sasso RC, Macadaeg K, Nordmann D, Smith M. Selective nerve root injections can predict surgical outcome for lumbar and cervical radiculopathy. *J Spinal Disord Tech* 2005;**18**:471–8.
4. Schutz H, Lougheed WM, Wortzman G, Awerbuck BG. Intervertebral nerve-root in the investigation of chronic lumbar disc disease. *Can J Surg* 1973;**16**:217–21.
5. Yeom JS, Lee JW, Park KW, Chang BS, Lee CK, Buchowski JM, *et al*. Value of diagnostic lumbar selective nerve root block: a prospective controlled study. *AJNR Am J Neuroradiol* 2008;**29**:1017–23.

Appendix 6　Studies included in the review of complications

1. Jönsson B, Strömqvist B, Annertz M, Holtås S, Sundén G. Diagnostic lumbar nerve root block. *J Spinal Disord* 1988;**1**:232–5.
2. Quinn SF, Murtagh FR, Chatfield R, Kori SH. CT-guided nerve root block and ablation. *Am J Roentgenol* 1988;**151**:1213–16.
3. Schutz H, Lougheed WM, Wortzman G, Awerbuck BG. Intervertebral nerve-root in the investigation of chronic lumbar disc disease. *Can J Surg* 1973;**16**:217–21.
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Appendix 7 Review protocol

Background

Prevalence and cost of low back pain

During each year 36 to 48% of UK adults recall having low back pain[1] [2] [3]. Lifetime prevalence has been estimated to be in the range of 58% to 62%[4] [2] [3]. In the UK the economic burden of back pain in terms of healthcare costs and lost productivity is around £12 billion[5]. In most acute cases seen in primary care, the pain is limited to the lower back and will resolve after a few days to a few weeks. However, some cases develop chronic pain and disability[6] and have referred symptoms of pain, sensory disturbance (e.g. numbness) and weakness extending to the buttocks, thigh or foot. In a minority of patients with low back pain, a diagnosis of lumbar radiculopathy is made when lower limb symptoms are thought to originate from inflammation or compression of the dorsal nerve root or ganglion.

Frequency of lumbar decompressive surgery and patient outcomes

Substantial numbers of patients with persistent low back pain are treated surgically. In 2008/9 there were more than 10,000 primary excisions of a lumbar intervertebral disc performed on NHS inpatients in England. Randomised trial evidence on the effectiveness and cost-effectiveness of lumbar discectomy in patients with radiculopathy and intervertebral disc herniation is not definitive. The SPORT trial randomised 501 patients to open discectomy or non-operative care[7]. Pain, physical function and disability improved substantially in both groups by 2 years, between group differences favoured surgery but were non-significant. Interpretation of the trial is hampered by substantial non-compliance (only 50% randomised to surgery received it) with treatment allocation. In 2008/9 there was one revision lumbar discectomy for every nine primary lumbar discectomies performed on NHS patients. Improved diagnosis could help identify patients most likely to benefit from surgery and minimise the cost and risks associated with unsuccessful back surgery.

Diagnosis of the cause of low back pain and the role of selective nerve root blocks

The exact cause of low back pain is often difficult to diagnose. In most patients, the diagnosis of radiculopathy is made by careful correlation of clinical signs and symptoms (e.g. pain distribution, paresis, straight leg raising test) and imaging findings (e.g. evidence of disc herniation and nerve root compression on MRI or CT myelography). But neither clinical findings[8] nor anatomical imaging have perfect diagnostic accuracy. Patients often find it difficult to precisely define the boundaries of their leg pain, sensory disturbance or weakness. MRI studies on volunteers have demonstrated surprisingly high rates of asymptomatic disc protrusions, extrusions, with associated nerve root compression[9]. Therefore clinical and imaging evidence of nerve root compression are frequently not completely concordant. In these cases, additional diagnostic tests such as selective nerve root blocks (SNRBs) could help clinicians and patients to choose between surgical and conservative care.

Selective nerve root blocks

SNRBs have been employed since the 1930s as a method of confirming the source of radicular pain prior to surgery [10]. Diagnostic SNRB consists of injection of local anaesthetic around spinal nerves under imaging guidance. Both provocative responses (replicating the patient's symptoms during needle placement) and analgesic responses (significant reduction of symptoms after injection) to SNRB may be diagnostically useful in confirming or ruling out a nerve root as the source of clinical symptoms. Recent international consensus statements have concluded that properly performed diagnostic SNRBs '…are useful when the location of symptoms seems to conflict with abnormalities identified with imaging findings…'[11], although the evidence on this topic was categorised as being of only moderate quality. The diagnostic value of SNRB should be weighed against the small risk of complications associated with

the procedure. A study of 1,777 procedures observed 98 (5.5%) transient post-procedure complications such as leg weakness or light-headedness[12]. More rarely, there are case reports of more serious complications, such as paraplegia[13].

The therapeutic impact and cost-effectiveness of selective nerve root blocks

The impact of 'diagnostic' SNRB results on treatment decisions is not well studied. Although not primarily designed to evaluate the therapeutic impact of diagnostic SNRB, data reported by Sasso et al suggest that only 8% of patients with a negative SNRB test subsequently had surgery at that lumbar level compared to 21% of patients with a positive SNRB ($p < 0.01$)[14]. These observational data are indicative, but cannot determine whether the SNRB result caused the change in treatment plan nor whether the differential treatment based on SNRB results improved patient outcomes.

We are not aware of any studies that have evaluated the potential cost-effectiveness of diagnostic SNRBs in patients considered for decompressive lumbar surgery. Primary excision of lumbar intervertebral disc procedures involve a mean inpatient stay of 3.2 days, totalling 30,738 days in English NHS hospitals annually. These acute costs, combined with additional NHS costs and productivity losses associated with rehabilitation from surgery, suggest that a minimally invasive test that accurately differentiates patients who will or will not benefit from surgery has the potential to be cost-effective.

Objectives

This evidence synthesis aims to determine whether selective nerve root blocks (SNRBs) result in more accurate diagnosis in patients considered for lumbar decompression surgery where there is doubt about the localisation of the lesion based on clinical signs and imaging findings (e.g. MRI). An economic model will evaluate the extent to which improvements in diagnostic accuracy lead to more cost-effective care for this patient group and subgroups within it. Specifically, the project will address the following objectives:

1. Systematic review to determine the relative diagnostic and prognostic performance of SNRB in addition to clinical and imaging findings to identify patients with lumbar radiculopathy who are good candidates for lumbar decompression surgery.
2. Evaluate whether the diagnostic and prognostic utility of SNRB varies by patient subgroups (e.g. patients with suspected radiculopathy at more than 1 level of the lumbar spine).
3. Systematic review to summarise the evidence on the incidence of procedure related complications of SNRB.
4. Review of previous economic studies of the use of SNRB in patients with suspected lumbar radiculopathy and a cost-effectiveness model to evaluate the efficiency of using SNRB in patients with discordant clinical and imaging findings, including value of information analysis.

Methods

Systematic review

A systematic review of the literature will be undertaken to determine the accuracy of SNRB in the diagnostic work-up of patients with suspected lumbar radiculopathy, who are candidates for decompressive surgery. The systematic review will be undertaken in accordance with the Centre for Reviews and Dissemination (CRD) guidelines for undertaking systematic reviews[15], and the Cochrane Handbook for Test Accuracy Reviews[16]. Using the same search strategy, we will separately identify studies reporting the incidence of adverse events associated with lumbosacral SNRB.

Search strategy and scoping exercise

A database of published and unpublished literature will be assembled from systematic searches of electronic sources, hand searching, and consultation with experts in the field. Studies will be identified by searching the following major medical databases: MEDLINE, EMBASE, Science Citation Index, BIOSIS Previews and LILACS. In addition, information on studies in progress, unpublished research or research reported in the grey literature will be sought from a range of relevant databases including Inside Conferences, Dissertation Abstracts and NTIS. Internet searches will also be carried out using Google Scholar. Attempts to identify further studies, including unpublished studies, will be made by contacting clinical experts and examining the reference lists of all retrieved articles. A draft search strategy was devised for MEDLINE in the OvidSP interface. The strategy combines terms for the selective nerve root blocks with terms for low back pain. We have not used a diagnostic filter due to problems associated with their use[17] and a desire to identify studies of SNRB related adverse events. The strategy will be validated further to ensure that it identifies all primary studies identified by previous literature reviews. The strategy will be converted to run appropriately on other databases. We will also use previous systematic reviews as a source of studies.

Planned inclusion/exclusion criteria

Studies that fulfil the following criteria will be eligible for inclusion in the systematic reviews:

	Review of diagnostic accuracy	Review of procedure related complications	Review of economic evaluations
Population	Patients with low back pain and symptoms in a lower limb	Patients with low back pain and symptoms in a lower limb	Patients with low back pain and symptoms in a lower limb
Target condition	Lumbar radiculopathy	Lumbar radiculopathy	Lumbar radiculopathy
Index test	Diagnostic SNRB administered under radiological guidance	Diagnostic SNRB administered under radiological guidance	Diagnostic SNRB administered under radiological guidance
Reference standard	Any reported reference standard, e.g. surgical findings and/or clinical outcomes	N/A	N/A
Outcome(s)	Sufficient data to construct contingency tables of index test versus reference standard. Data will be extracted at the patient level, unless unavailable, and then injection level will be used.	Transient and permanent adverse events	Cost effectiveness, cost utility, cost benefit, cost consequence
Study design	Diagnostic cohort or within-patient case-control studies	Any study design except case-reports on which included less than 15 patients.	RCTs, controlled studies, decision analyses

Our scoping exercise suggested that several reference standards (e.g. surgical findings, pain response to active and control SNRB injection) had been used in the literature, but that there is no agreed gold standard. We will include all diagnostic accuracy studies in our narrative systematic review which will allow a broad critique of the strengths and weaknesses of each reference standard reported in this literature.

Assessing relevance and inclusion

The results of the searches will be screened for relevance independently by two reviewers. Disagreements will be resolved through consensus or referral to a third reviewer where necessary. Studies that appear potentially relevant will be ordered and assessed for inclusion by one reviewer and checked by a second.

Data extraction

Data extraction forms will be developed using Microsoft Access. These will be piloted on a small selection of studies and adjusted as necessary. Study data will be extracted by one reviewer and checked by a second. Disagreements will be resolved through consensus or referral to a third reviewer where necessary. Data will be extracted on the following: study details (identifier, study design, location, year), participant details (number of participants, age, gender, details of previous tests received, other relevant details), index test details, comparator test details (where reported), reference standard details and contingency tables of test performance. We anticipate that most diagnostic accuracy studies will present data only on SNRB. However, where presented, we will also record the diagnostic accuracy of clinical findings and imaging findings (e.g. CT myelography or MRI) alone or in combination with SNRB. Data will be extracted and analysed at the patient level (unless unavailable, and then injection level will be used). Where injection level data are used we will use an approximate correction to the standard errors if necessary to avoid overstating precision and giving disproportionate weighting such studies. For the review of adverse events, we will abstract data on the type, number, severity and duration (acute/chronic) of adverse events.

Quality assessment

Diagnostic accuracy studies will be assessed for methodological quality using an updated version of the QUADAS tool [18]. This tool includes domains on patient selection, index test, reference standard, and patient flow and timing and assesses primary studies in terms of risk of bias and applicability to the review question. Quality assessment forms will be developed using Microsoft Access. Quality assessment will be carried out independently by two reviewers. Disagreements will be resolved through consensus or referral to a third reviewer where necessary.

Statistical analysis

The statistical analysis will in general follow the recommendations in Chapter 8 of the draft Cochrane Handbook for Test Accuracy Reviews[16]. Prior to data synthesis, the project team will meet to review all reference standards reported in the literature. The project team will create a hierarchy of reference standards from most to least valid. Diagnostic accuracy studies using reference standards considered invalid will be described and critiqued, but not included in the evidence synthesis. Our recommendations for current practice will be based on studies using the best available reference standards. The range in sensitivity, specificity, likelihood ratios (of both positive and negative tests results) and diagnostic odds ratios (DORs) will be calculated and discussed, together with possible ranges in positive and negative predictive values which will be calculated based on a number of different estimates of disease prevalence. Confidence intervals for sensitivity, specificity, likelihood ratios and DORs in individual studies will be displayed using forest plots. We will stratify our analysis by study design (case control versus cohort) as the potential biases associated with case control studies on this topic (e.g. spectrum bias) are very different to the potential biases in the cohort studies (e.g. partial verification bias).

To assess whether results vary, results will be stratified according to relevant patient subgroups reported either within or between studies. A priori patient subgroups of interest are patients with suspected single versus multi-level radiculopathy and patients with suspected disc versus bony stenosis of the neural foramen. The policy implications of using SNRB in each patient subgroup will be assessed by developing separate cost-effectiveness models for each subgroup using subgroup specific estimates of SNRB sensitivity and specificity.

The extent of data pooling and meta-analysis will depend on the number of sufficiently homogenous diagnostic accuracy studies identified. If meta-analysis is feasible, summary ROC plots (SROC plots) will be used to display sensitivity and specificity using different symbols or separate plots for different test types or combinations of tests. Formal analyses will use bivariate and hierarchical summary ROC (HSROC) models, which the applicants have shown to be identical in the absence of covariate effects[19]. These statistically rigorous approaches allow estimation of summary sensitivity, specificity, likelihood ratios and DORs with associated confidence intervals or regions.

They also allow estimation of summary ROC curves and prediction regions for the true sensitivity and specificity in a future study.

Most of the analysis will be conducted in Stata version 10, using a command for meta-analyses of test accuracy studies (metandi). We will also use the NLMIXED procedure in SAS for the HSROC model with covariates if required.

Adverse events associated with SNRB will be classified as temporary or permanent. The type and frequency of adverse events will be calculated and discussed. Estimates and confidence intervals for complication rates in individual studies will be displayed using forest plots.

Review of previous economic studies

The search strategy for identifying SNRB diagnostic accuracy studies will also be used to identify studies investigating the cost and outcomes of diagnostic SNRB. Titles and abstracts will be reviewed, focussing on economic evaluations of SNRBs in patients with radiculopathy considered for decompressive surgery.

The quality of any primary economic evaluations identified will be assessed using the Quality of Health Economic Studies (QHES) instrument [20]. We will use the Philips checklist [21] to describe the strengths and weaknesses of existing cost-effectiveness decision analysis models. We will provide a qualitative summary of the findings of all previous economic evaluations. Based on our scoping exercise we anticipate that there will be very few, if any, full economic evaluations, especially in an NHS setting. Therefore, we will develop a decision analytic economic model based on the best evidence on costs, diagnostic accuracy, therapeutic impact and health outcomes.

Development of an Economic Model

A decision analytic model will be developed to estimate the cost-effectiveness of SNRB in patients with suspected lumbar radiculopathy who are thought to be suitable for lumbar decompressive surgery. If the systematic review and meta-analysis reveal important differences in the diagnostic accuracy of SNRB by patient subgroup, we will develop separate models for each subgroup (e.g. multiple versus single-level radiculopathy). In developing the model, we will follow the best-practice principles suggested by Buxton and colleagues[22]: 1) The model will be kept as simple as possible to aid understanding by decision makers; 2) The presentation of methods and results will be as transparent as possible; 3) The quality of all data used in the model will be explicitly discussed; 4) Uncertainty in the model will be explored using probabilistic sensitivity analysis; 5) The model will be validated against other models and epidemiological studies.

Additional literature searches will be undertaken to help populate the decision model. We anticipate that the key parameters in the model will include: 1) the pre-SNRB prevalence of nerve root compression; 2) the cost of SNRB; 3) SNRB related complications; 4) the sensitivity and specificity of SNRB; 5) the impact of the SNRB result on the decision to perform surgery or the surgical approach selected; 6) the cost of surgery and conservative care; 7) the effectiveness (quality adjusted life years) of surgical and conservative therapy at reducing morbidity in patients with true positive, false positive, true negative and false negative SNRB test results; and 8) productivity losses to society due to symptom related incapacity.

Some of the model parameters, for example prevalence, SNRB complications and diagnostic accuracy, will be directly informed by our systematic reviews. For other parameters, such as the cost of SNRB and therapy, we will use routine data (e.g. NHS reference costs) and information from NHS acute trust finance departments to derive a range of cost estimates. The primary analysis of the effectiveness of surgical and conservative therapy will be based on EQ-5D outcomes reported in the SPORT RCTs[7]. Because substantial non-compliance with random allocation affected the SPORT results, we will conduct separate sensitivity analyses using both the 'as treated' and 'intention-to-treat' effect sizes. We will access SPORT data under the NIH data sharing guidelines.

In the primary analysis, we will calculate cost-effectiveness from the perspective of the NHS and Personal Social Services, excluding costs incurred by patients, employers and other agencies. Secondary analysis will broaden this to the societal perspective. We will compare the incremental cost effectiveness adding SNRB to the standard diagnostic workup of clinical findings and radiological imaging. The project economists and clinicians will jointly review the structure of the final model to ensure that it reflects the most clinically plausible diagnostic and therapeutic transitions. Extreme value sensitivity analyses will be used to test the internal consistency of the model. The model will consist of two parts. The first (short-run) sub-model will consider the incremental cost per correct diagnosis of SNRB. The short-run model will incorporate point estimates of diagnostic accuracy and a distribution reflecting the range of parameter uncertainty from the systematic review. Estimates of sensitivity and specificity will be combined with the pre-test prevalence of true nerve root compression to generate post-test probabilities of appropriate surgery. This results in four possible short-run outcomes: positive SNRB result in a patient with radiculopathy caused by nerve root compression (true positive), positive SNRB result in a patient whose symptoms are not caused by nerve root compression (false positive), negative SNRB result in a patient with radiculopathy caused by nerve root compression (false negative), and negative SNRB result in a patient whose symptoms are not caused by nerve root compression (true negative).

The second (long-run) element of the model will extrapolate the long-term costs and health effects of SNRB. The long-run model will use a decision tree and Markov process to track the transition of patients between various post-treatment health states (e.g. Good/moderate/poor outcome and death), return to work and the requirement for further therapy (e.g. re-operation). All parameters will be entered into the model as point estimates with distributions reflecting the degree of statistical certainty based on current evidence. The model will initially track costs and outcomes over a four year time horizon to match the outcomes time frame reported by the SPORT trial and then extrapolate over a longer term based on several assumptions about the continuation of the benefit of surgery after the end of the SPORT trial. Costs and outcomes in future years will be discounted at an annual rate of 3.5% and varied between 0% and 6% in sensitivity analysis to account for methodological uncertainty. The main outcome of the model will be the incremental cost per Quality Adjusted Life Year (QALY) of using SNRB in addition to clinical findings and imaging. Probabilistic sensitivity analysis (PSA) will be undertaken to reflect all parameter uncertainty in the model using Monte Carlo simulation. Results will be plotted on the cost-effectiveness plane and expressed using cost-effectiveness acceptability curves and net monetary benefit.

Expected Value of Information (EVI)

The systematic review and economic model will be used to make recommendations for optimal use of SNRB based on current evidence. But evidence is incomplete and further research may be valuable. Expected value of information analysis (EVI) uses the best available evidence (and the uncertainty that surrounds it) to estimate the expected benefit of future research[23]. Research recommendations (and funding decisions) can then focus on research areas where the benefits of future research, by reducing uncertainty, most clearly outweigh the costs of that research. We will use Monte Carlo simulation to obtain EVI estimates from the decision analysis model on the partial expected value of perfect information (pEVPI) and partial expected value of sampled information (pEVSI)[24]. The former estimates whether any amount of further research on a topic (e.g. the sensitivity and specificity of SNRB) is likely to change the optimal diagnostic strategy. The latter estimates the expected benefit of conducting a new research project (e.g. diagnostic accuracy study of SNRB) with a given sample size. EVSI can be compared between different types of research (e.g. a diagnostic accuracy study of SNRB versus an RCT of lumbar discectomy) to establish priorities.

Project Timetable and Milestones

Project start	Month 1	Oct, 2010
Protocol development	Month 1	Oct
Literature searching (including economic data)	Months 2–5	Nov–Feb
Develop economic model structure(s) for review	Months 1–4	Oct–Jan
Protocol peer review	Month 2	Nov
Relevance screening	Months 4 and 5	Jan–Feb
Inclusion assessment	Months 6 and 7	Mar–Apr
Populate economic model with parameters	Months 5–7	Feb–Apr
Data extraction and quality assessment	Months 7 and 8	Apr–May
Systematic Review and Meta-analysis	Months 9–11	Jun–Aug
De-bug economic model, conduct SA and EVI analysis	Months 9–13	June–Oct
Report production	Months 13–15	Oct–Dec
Draft report to advisory panel	End of Month 14	Nov 30, 2011
Deadline for comments on report from advisory panel	Middle Month 15	Dec 15, 2011
Submit final report	End of Month 15	Dec 31, 2011

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