Cost-effectiveness and quality of life after treatment of lumbar spinal stenosis with the interspinous distractor device (X-STOP) or laminectomy:

a pilot study

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MD(Res)

By Mr Besnik Nurboja, MBBS BSc MRCS

Institute of Neurology

University College London

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Declaration

I, Dr Besnik Nurboja confirm that the work presented in this thesis is my own. Where information is derived from other sources, I confirm that this has been indicated in the thesis. The work for this thesis is carried out in the Department of Neurosurgery at the National Hospital for Neurology and Neurosurgery, Queen Square, London. This work was supervised by my mentor Mr David Choi, Consultant Neurosurgeon. This project was approved by the Ethics Committee and all the subjects were consented prior to recruitment in the study.

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Abstract

OBJECTIVES: Primary end-point was to assess the cost-effectiveness of lumbar laminectomy versus X-stop insertion in patients with neurogenic claudication secondary to LSS. Secondary end-points were to compare quality of life, clinical outcomes, radiological parameters and complications within two groups. This is a pilot study to produce predictive models and allow sample size calculation.

DESIGN: Multicentre randomised trial with two interventional arms, namely the lumbar laminectomy(LL) and X-stop(XS) groups.

METHODS: Patients were recruited from two neurosurgical centres after fulfilling eligibility criteria and followed up for 1 year. Self-reported general quality of life and disease-specific questionnaires were used. The assessments were performed at discharge, 6 weeks, 6 and 12 months. Also, radiological parameters were analysed.

RESULTS: In this pilot study 26 patients were identified of which 6 were excluded and 20 were randomised with 10 in lumbar laminectomy and 10 in X-stop(XS) group from June 2008 to January 2010. LL group incured lower costs than the XS group but showed no significant between-group differences in utility values (QALYs). We found that LL was perhaps more cost-effective than the XS but with uncertainty, suggesting the need for a larger trial. There were no significant differences between the two groups in quality of life, clinical outcomes or success rates but within group improvements were found. Importantly, 6 out of 10 patients (60%) from XS group crossed over to LL group.
Sample size calculation with the original data showed the need for 25 patients in each arm to detect clinical significance in future clinical trial.

CONCLUSION: Our results suggest that LL is possibly cheaper and more cost-effective than XS over a 1-year period, in National Health Service. No significant differences in quality of life and clinical outcomes between the two procedures were detected although this is only a pilot study with a small sample size.

Table Of Contents

List of Figures

Page no

List of Tables

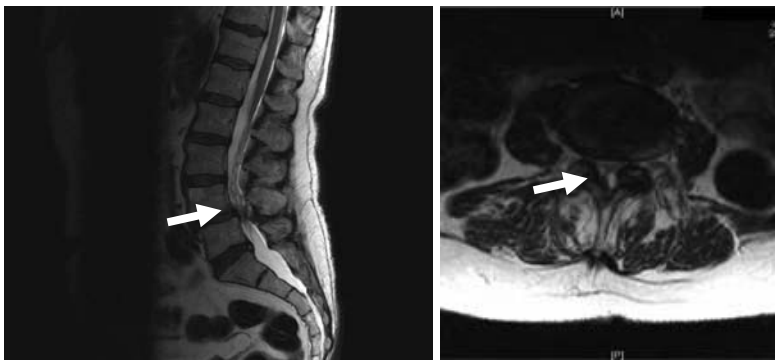
Page no

Abbreviations

ASA	American Association of Anaesthetists
BMP	Bone Morphogenetic Protein
BP	Bodily pain
CBA	Cost-benefit analysis
CER	Cost Effectiveness Ration
CRF	Case Report Form
EMG	Electromyography
EQ5D	EuroQol Questionnaire
GH	General health
ICER	Incremental Cost-effectiveness ratio
IPD	Interspinous Distraction Devices
HRQOL	Health Related Quality of Life
LBP	Low Back Pain
LL	Lumbar laminectomy
LSS	Lumbar Spinal Stenosis
MH	Mental health
NIC	Neurogenic Intermittent Claudication
ODI	Oswestry Disability Index
PF	Physical functioning
QoL	Quality of life
RCT	Randomised Controlled Trial
RE	Role emotional
RP	Role physical
SF36	Short Form 36
SF	Social functioning
VAS	Visual Analogue Scale
VT	Vitality
XS	X-stop device
ZCQ	Zurich claudication questionnaire

1. INTRODUCTION

1.1. **Definition:** - Lumbar stenosis is defined as the reduction in the diameter of the spinal canal, lateral nerve canals, or neural foramina, associated with a complex of clinical signs and symptoms comprising back pain and stress related symptoms (pain, paraesthesia) in the legs (claudication).



A) B)

Figure 1.1: MR images T2 –weighted sequences of lumbar spine showing the stenotic segment at the L4/5 level (white arrow): A) Sagittal view; B) Axial view.

1.2. **Epidemiology:** - The annual incidence of degenerative lumbar spinal stenosis (LSS) is reported to be 5 cases per 100,000 individuals. This is 4-fold higher than the incidence of cervical spinal stenosis.(1)

LSS has become the most common indication for lumbar spine surgery, in part because of the increasing quality and availability of radiological imaging.(2)

The increasing frequency of LSS surgery seems to reflect the elevated demand for mobility and flexibility in the aging population. (3)(4)(5)

1.3. **Cost burden: -** Loss of productivity at work represents the majority of the costs associated with LSS, the economic burden of which is estimated to exceed US$100 billion. (6).

1.4. **Historical perspective: -** Sachs and Fraenkel, 1900 (7) and Baily and Casamajor, 1911 (8) are the first to describe lumbar spinal changes leading to spinal stenosis and nerve root compression with supporting evidence provided by Elsberg (9) and Kennedy (10) describing that thick laminae, hypertrophied articular facets, and thickened ligamentum flavum lead to spinal stenosis and nerve root compression.

Neurogenic claudication, as a classical symptom of LSS, was a term coined by Dejerine (1911) (11) and defined by von Gelderen (1948) (12) and, later, Verbiest (1954). (13) Van Gelderen (1948) described LSS as localized, bony discoligamentous narrowing of the spinal canal that is associated with a complex of clinical signs and symptoms comprising back pain and stress related symptoms in the legs.(12) This description is still used today.

Schlesinger and Taveras (14) were the first to emphasize that the dimension of the spinal canal was more important than the size of the disc protrusion in the production of symptoms in patients with herniated discs and concomitant multiple root and cauda equina compression.

Verbiest (13) (15) (15) was the first to define the pathomorphologic changes specifically the encroachment of the canal by hypertrophied articular processes, and called attention to the characteristic clinical manifestations of the condition including neurogenic claudication.

The progressive pathologic changes that occur in the three joint complex of the disc anteriorly and the zygoapophyseal joints posteriorly as well as the natural history of the condition were described initially by Kirkaldy-Willis (1983). (16) (17)(18)

1.5. **PATHOPHYSIOLOGY**

There are two postulated mechanisms of degenerative lumbar spinal stenosis: *the molecular mechanism* and *the mechanistic mechanism.*

1.5.1. **The molecular mechanism:** The putative substance responsible for bone degeneration and osteophyte formation remains elusive. Bone Morphogenetic Proteins (BMPs) are multipotent proteins that regulate the growth, differentiation, and programmed death (apoptosis). They are abundantly present in cartilage and bone. BMPs and their receptors are greatly expressed during maturation of the intervertebral disc and seem to be related to chondrogenesis within the disc. As the disc degenerates, BMPs and its receptors migrate from the hyaline cartilage of the vertebral endplate to fibrous cells within the annulus and to the calcified cartilage at the site of the enthesis and thus may be related to the formation of osteophytes. It also is suggested that the BMPs, by mediating an effect on cellular apoptosis, contribute to the degenerative process because it has been clearly shown that apoptosis plays a pivotal role in disc degeneration.(19)

The LSS is caused by remodeling and overgrowth of bone with osteophyte formation. It is thought that the degenerative process initiates or accelerates the bony overgrowth affecting the three joint complexes, which comprises the two zygoapophyseal joints and the adjoining disc. (18) Commonly, the degenerative process starts in the disc and affects the articular processes secondarily. Loss of tissue (e.g.from articular cartilage chafing due to friction), synovitis, or loss of disc height results in relative ligamentous laxity and accelerated joint degeneration. Interestingly, the remodeling of the bone can be considered either as a reaction to the excessive joint motion or a physiologic attempt for local arthrodesis, leading to end of result of decreased segmental mobility. However, decreased mobility in one segment generates abnormal stress forces on adjacent spinal segments, causing them to degenerate at an accelerated rate.

The association between the degenerative process and mobility arises from the fact that the two lower motion segments (L3-L4, L4-L5), which are the most mobile in lumbar region, are most commonly affected by degenerative

stenosis. The L5-S1 has a relatively large L5 transverse processes with strong ligamentous attachments to the iliac crest.

Bone morphogenetic proteins (BMPs) are the cytokines of the TGF- superfamily that have been implicated in the process of disc degeneration.(20) (21)

1.5.2. **The mechanistic mechanism:** Numerous factors can contribute to the development of spinal stenosis. These can act synergistically to exacerbate the condition. Degeneration of the vertebral disc often causes a protrusion, which leads to ventral narrowing of the spinal canal. As the disc degenerates, the height of the intervertebral space is further reduced, which causes the recess and the intervertebral foramina to narrow, exerting strain on the facet joints causing their hypertrophy.(22)

In addition, as a result of the reduced height of the affected spinal segment, the ligamentum flavum forms creases, which exert pressure on the spinal dura from the dorsal side. Loosened ligaments concomitantly propagate hypertrophic changes and osteophytes, creating the characteristic trefoil-shaped narrowing of the central canal. (23)(24) (22) (25) (26) (27) (28) (29)

1.6. PATHOLOGICAL ANATOMY

Degenerative lumbar spinal stenosis is a spectrum of the following conditions: central canal stenosis, lateral spinal stenosis and intervertebral foraminal canal stenosis.

Central stenosis is caused by hypertrophy of the facet joints, ligamentum flavum, disc protrusion, spondylolisthesis, or by a combination of these. (30) (31)
Hyperextension of the lumbar spine increases the extent of compression because of the effect of additional narrowing of the spinal canal. By contrast, hyperflexion results in widening of the spinal canal. It is shown that LSS is frequently exacerbated further by vertical load. (32)
Indeed, epidural pressure is elevated while standing or walking, and lowered when sitting and in flexion.(33)(34) Experimental animal models have been developed to investigate the underlying pathophysiology of LSS in more detail (35) and to test pharmacological interventional strategies. (36) In one such experimental model for spinal canal stenosis, a piece of silicon is placed under the lamina at L4 level in young adult rats. Thus this model would perhaps be more relevant to acute cord compression rather than chronic conditions. Furthermore, biomechanics of quadripedal rats is different from those of bipedal patients.

Stenosis at multiple levels is more common than strictly segmental stenosis. In approximately 40% of cases, central stenosis is caused by soft tissue hypertrophy. On computed tomography (CT) scans, midsagittal lumbar canal diameters less than 10 mm represent absolute stenosis and midsagittal lumbar canal diameters less than 13 mm represent relative stenosis.(37)

LSS can also be subdivided into relative and absolute according to the anterior–posterior diameter of the spinal canal. Relative LSS (10–12 mm diameter in spinal canal; physiological value is 22–25 mm) is usually asymptomatic,

whereas absolute LSS (spinal canal <10 mm in diameter) is often symptomatic and is associated with absence of free subarachnoid space.
The most common symptom associated with LSS is neurogenic claudication, which comprises limping or cramping lumbar pain that radiates into the legs primarily during walking. Degenerative LSS can ultimately lead to the compression of individual nerve roots, the meninges, the intraspinal vessels, and, in exceptional cases, the cauda equina (Figure 2). (38)
Nerve root compression triggers localized inflammation, which affects the nerve root's excitatory state. (39)

Lateral spinal stenosis is a common cause of lumbar radiculopathy. The nerve root canal has been divided into three anatomic zones: the entrance zone, the midzone, and exit zone.(40)

The entrance zone is the subarticular zone medial to the pedicle and is synonymous with the lateral recess. Its borders consist laterally of the pedicle, posteriorly of the superior articular facet, anteriorly of the posterolateral surface of the vertebral body caudally and the disc rostrally, and medially by the thecal sac. The root sleeve containing cerebrospinal fluid covers the nerve root at the entrance zone. Lateral to the entrance zone the nerve root sleeve coalesces with the nerve root and is devoid of cerebrospinal fluid. The minimal height of a normal lateral recess is 5 mm; a height of 3 to 4 mm is suggestive of lateral recess stenosis and a height of 2 mm is considered pathologic.(41)

The majority of cases of lateral recess stenosis are produced by posterolateral disc protrusion or hypertrophy of the superior articular process also referred to as lateral recess syndrome.

The midzone is the part of the canal beneath the pars interarticularis and just inferior to the pedicle where the nerve root takes an oblique downward course from the lateral recess to the foramen. Anteriorly, the midzone is bordered by the posterior aspect of the vertebral body, posteriorly by the pars interarticularis and medially by the opening to the spinal canal. Computed tomography scans

accurately show the pars interarticularis and its relationship to the underlying nerve root.(42)

A T1- weighted parasagittal magnetic resonance imaging (MRI) scan defines the pars as a high signal intensity bone marrow surrounded by the lower signal of the cortical bone. The bone marrow signal remains continuous from the superior to the inferior articular process. An interruption of this signal is indicative of a pars defect.(43)(44)

The most common causes of midzone nerve root compression include a pars defect or pedicular compression. A pars defect such as in isthmic spondylolisthesis with fibrocartilaginous tissue overgrowth can cause nerve root entrapment. More common in patients with rotational deformities or spondylolisthesis is kinking of the nerve root situated inferomedially to the pedicle by one pedicle that is lower than the other because of a rotation deformity or asymmetric disc collapse.

The exit zone corresponds to the intervertebral foramen. It is bordered superiorly and inferiorly by the pedicles of adjacent vertebrae, posteriorly by the pars interarticularis and ligamentum flavum, and anteriorly by the posteroinferior and posterosuperior aspects of the adjacent vertebral bodies and intervening disc. The foramen is shaped like an inverted teardrop; its normal height varies from 10 to 23 mm and its width at the upper foramen varies from 8 to 10 mm. A foraminal height of less than 15 mm and a disc height of less than 4 mm are associated with nerve root compression 80% of the time. The ventral and dorsal nerve roots occupy 23% to 30% of the foramen and lie anterior to the dorsal root ganglion. The dorsal root ganglion usually is located in the superior lateral aspect of the foramen directly below the pedicle in 90% of lumbar levels.(45) Parasagittal T1-weighted MR images readily define the integrity of the foramen. The nerve root proper has a low signal and is surrounded by the higher intensity signal of fat. Obliteration of the fat pad often is indicative of foraminal stenosis.

1.7. Natural course of the disease

LSS is a degenerative condition that develops slowly over time, with neurological deficits being usually only subtle. It is usually diagnosed in patients over the age of 50 years. There are, however, no prospective long-term studies that document the natural symptomatic changes over time.(46) This makes the initiation and choice of a specific therapy difficult, as such decisions ideally require an estimate of the natural course of the condition. (4) .

The Spine Patient Outcomes Research Trial (SPORT) reported that there was no worsening of symptoms over 2 years in most patients in the conservatively treated control group. (47) Another study reported an increase in the severity of symptoms in ~20% of the untreated cases, (46) whereas a further trial focusing on pain development over almost 5 years found that the clinical symptoms of 70% patients reached a plateau, 15% experienced pain exacerbation and 15% spontaneously improved. (22) (48)

1.8. Clinical Features

Onset: - Usually manifests in patients in the sixth or seventh decade of life. The congenital form of spinal stenosis or canal and lateral recess stenosis usually manifest in patients in the third or fourth decade of life.

Gender: - LSS has a slight preponderance in women.

Levels affected:- Degenerative spinal stenosis most commonly affects the L3-L4, and L4-L5 segments to cause cauda equina compression.

Clinical features: - Some patients with stenosis primarily compressing a nerve root have symptoms of a radiculopathy but most experience a combined mixed symptomatology.

- *Pain:* - Radicular pain is localized better, may be claudicant and neurogenic, and can be associated with weakness in specific well-localized muscles or dermatomal sensory changes. One or several nerve roots may be involved, occasionally segmentally separated, and sometimes both lower limbs are affected.
Lower extremity pain is present in approximately 80% of patients and back pain is present in approximately 65% of patients. Pain is often poorly localized and frequently associated with paresthesias.

-*Other symptoms:* - Patients describe their symptoms as a discomfort ranging from a rubberlike feeling, leg weakness to actual pain in the back, buttocks, thighs, and legs.

- *Spread of symptoms:* - Symptoms may ascend from the distal lower extremities to the buttock, or alternatively descend the lower extremity.

-*Localisation of symptoms:* - There is generally a bilateral distribution but can be also be unilateral. Symptoms may not be symmetric and may affect the entire limb or parts thereof. The back pain is localized to the lumbar spine and can radiate towards the gluteal region, groin and legs. In cases of lateral recess stenosis or foraminal stenosis, isolated radiculopathy can occur.
- *Relationship between symptoms and level of activity (Neurogenic claudication*):-
Neurogenic claudication is the most specific symptom of LSS (4) although it is nearly always accompanied by further symptoms mainly pain but also paraesthesias. This is considered a pathognomonic aspect of lumbar stenosis as a relationship between symptoms and function. Symptoms are likely to manifest on prolonged standing or walking and decrease when the individual stops the provoking activity and rests. As the disorder progresses however, the individual's time of activity before symptoms manifest shortens. Because of the clinical similarity to claudication caused by vascular insufficiency of the lower extremities, the lumbar stenosis pain syndrome has been termed pseudoclaudication or neurogenic claudication.(49)(50)

There are three prevailing theories that explain neurogenic claudication: **the ischemic theory, the mechanical compression theory** and **the theory of stagnant anoxia.**

The ischemic theory: This theory postulates that as metabolic demands increase during activity such as walking, this increased demand cannot be met because of an insufficient blood flow secondary to segmental compression. A relative nerve root ischemia ensues and may lead to pain, sensory loss, and a motor deficit.(51)
In support of the vascular insufficiency theory is the fact that the intrafascicular microvascular matrix is predisposed to decrease in diameter and flow as a result of stretch and vessel angulation caused by bone overgrowth and stenosis. Under normal conditions, nerves are tolerant of traction because the intrafascicular arterial branches have compensating coils that can elongate on traction. In stenosis, acute angulation and tethering of the neural elements restrict the intrafascicular micromovement associated with traction, which results in narrowing of the blood vessels and diminished blood flow.(52)
Conversely, compressive radiculopathy can cause autonomic impairment resulting in impairment of circulation in the legs. (53)

The mechanical compression theory: The fact that many patients with claudication attributable to cauda equina dysfunction have symptoms commensurate with posture rather than activity, has advanced the mechanical compression theory. In many such patients, assuming a lordotic posture is sufficient to provoke symptoms that are alleviated by flexion.(54)

The theory of stagnant anoxia: This theory may reconcile the vascular and mechanical-compressive hypotheses and explain the appearance of symptoms in static and dynamic conditions. In this hypothesis, the mechanical compression by bone and soft tissues may compress the neural elements, the draining veins that exit the canal with the spinal roots or cause cerebrospinal fluid entrapment, thus resulting in interference with venous return.(55)
This dynamic entrapment of cerebrospinal fluid and ensuing increase in fluid pressure occurs distal to the site of narrowing or compression within a segment constricted rostrally and caudally by a two level stenosis. This increase in

cerebrospinal fluid pressure may impede with the radicular venous return to culminate in relative hypoxia, or cause a reduction in the metabolic exchange and nutritional supply to the roots.

- *Relationship between symptoms and posture:* - Often, patients with spinal stenosis assume a characteristic posture either standing erect or in a flexed forward position. The stooped posture occurrence is attributed to two changes to spinal column at the affected levels. In flexion, the vertebral canal lengthens and the spinal roots stretch. In extension, the canal shortens and the roots undergo an increase in their total volume. In addition, increase in spinal lordosis by trunk extension increases the bulging of the ligamentum flavum and intervertebral discs into the spinal canal and thereby compromises the size of the canal additionally. The onset of symptoms in the lower limbs after prolonged standing and their improvement on sitting, lying with the legs flexed, flexing at the waist, or squatting all are presumably attributable to the same mechanism.

-*Autonomic dysfunction: -* Autonomic-sphincter dysfunction manifesting as recurrent urinary tract infections associated with an atonic bladder, incontinence, and more rarely, episodes of urinary retention are not infrequent and occur in approximately 10% of patients mainly with advanced stages of spinal stenosis. Other and rarer autonomic symptoms have been described, and in general autonomic dysfunction responds favorably to decompression.(56)
In addition, as previously mentioned, compressive radiculopathy can cause autonomic dysregulation and impaired circulation in the legs.(21)

- *Neurological signs:-* A paucity of neurologic findings on physical examination, often despite a history of severe disability, is typical for patients with spinal stenosis. Furthermore, characteristic for the condition is the development of neurologic signs when the patient becomes symptomatic after a period of activity (walking) that provokes the symptoms. The most common findings are of deep tendon reflex changes, sensory loss, and muscle weakness. Straight leg raising rarely is positive, but flattening of the lumbar lordosis and a decrease in lumbar extension are common findings. Lasegue testing (a passive leg flexing test) often remains negative in patients with LSS and is frequently accompanied by a feeling of ‘heavy legs’, a characteristic sign of LSS.

Diagnosis of LSS is hampered by a number of frequent comorbidities such as peripheral neuropathies, which can themselves be relevant differential diagnoses.

-*Depression:-* Approximately 20% of patients with LSS exhibit symptoms of depression and 25% are dissatisfied with their life before surgery, a similar pattern to that seen in patients with other chronic disorders. (57)(58)
Evaluation of mood and contentment in patients is important, as both can markedly differ between patients with LSS and healthy controls, and can influence diagnostic and therapeutic decisions. Patient reported symptoms—even those that are transient in nature should be considered seriously in the diagnostic workup, especially during initial consultations.

- *Grading of LSS based on symptoms:*
Three grades of LSS have been described. (59).

- Grade I (neurogenic claudication): - characterized by a reduced walking distance (caused by pain) and sensory-motor deficits that at rest might be unremarkable, but can deteriorate while walking. However, not all patients with LSS exhibit symptoms consistent with neurogenic claudication, which is why other classifications of LSS exist.
- Grade II (Neurogenic paresis):- refers to already persistent sensitivity deficits, loss of reflexes and neurogenic paresis.
- Grade III is reached if persistent, progressing paresis is present, accompanied by partial regression of pain.

-*Correlation of clinical symptoms to radiological findings: -* The scarcity of neurologic findings is in marked contrast to the profound changes seen on myelography, CT scans and MRI scans. The history rather than the objective clinical findings and imaging studies are the decisive factor in establishing the diagnosis.

- *Correlation of clinical symptoms to neurophysiological findings: -* Of the ancillary laboratory studies that may be helpful in the diagnosis, except for imaging studies, is the neurophysiologic investigation. The results of electromyography will be abnormal in the majority of patients. Electromyography is considered more sensitive than the neurologic

examination. Abnormalities seen on electromyography consist of denervation in muscles innervated by lumbosacral nerve roots. Findings often are bilateral and are located in the paraspinal area.

1.9. **Differential diagnosis**

The differential diagnosis of spinal stenosis includes disc herniation and neoplasia that can be ruled out by imaging studies. More perplexing is the differentiation between neurogenic claudication attributable to cauda equina compression and claudication attributable to peripheral vascular disease. There often is an overlap in the two conditions. Vascular Neurogenic claudication causes pain that is more cramp-like, there is absence of one or more peripheral pulses, and often there are trophic changes in the extremities. Worsening neurologic symptoms and signs after ambulation or with an increase in the lordotic posture of the spine and/or relief of symptoms with a change in posture alone while exercise continues suggests neurogenic claudication (Table 1.1.). Walking-induced symptoms of neurogenic claudication often disappear when the patient sits or are relieved after a few minutes of rest. In vascular claudication, lower extremity symptoms often decrease or disappear even simply on standing or walking.

Osteoarthrosis of the hips may mimic spinal stenosis because of similar gait disturbance and buttock and proximal thigh pain.

Careful examination of the hips is recommended and occasionally radiographs of the hips are warranted. Gait disturbance and bladder incontinence are prominent symptoms of normal pressure hydrocephalus, a condition affecting patients in the same age range as those patients who are affected with spinal stenosis. Pain is not a feature of normal pressure hydrocephalus, the gait is characteristically shuffling and cognitive dysfunction is common. A non-contrast CT scan or MRI scan of the brain readily rules out this condition.

In contrast to the situation in LSS, hyposensibility resulting from peripheral neuropathies usually exhibits a bilateral distal stocking-shaped pattern, irrespective of posture, rest or physical stress. Iliosacral joint disorder occasionally mimics LSS, with low back pain radiating to the buttocks and the thighs when standing and walking.

Unlike LSS, iliosacral joint pain is characterized by tenderness of the joint.

Sphincter involvement is very rare in LSS, as the sacral nerves are relatively

protected from compression owing to their central position within the cauda equina. (46)

In patients exhibiting vesicorectal voiding and upper motor neuron signs (for example, Babinski's reflex and hyperreflexia), cervical or thoracic myelopathy needs to be ruled out. Neuroradiological assessment when performing radiological assessment of LSS, some inherent problems with imaging of the lumbar spinal canal need to be considered.

DIFFERENTIAL DIAGNOSIS:

■ Neurogenic claudication or vascular claudication
■ Radiculopathies or polyneuropathies
■ Intraspinal synovial cyst
■ Disc prolapse
■ Tethered cord or spina bifida
■ Coxarthrosis or arthrosis of the iliosacral joint
■ Abdominal aortic aneurysm
■ Neoplasia (for example, tumor, spinal roots, meninges, bones or filiae)
■ Inflammatory conditions (for example, spondylodiscitis, arachnoiditis)
■ Dissociative syndromes

TABLE 1.1. Comparison of Vascular and Neurogenic Claudication (63)

Signs and Symptoms	Vascular	Neurogenic
Claudication distance	Fixed	Variable
Type of pain numbness	Cramps, tightness	Dull ache,
Relief at cessation	Immediate	Lingers for a of activity few minutes
Back pain	Rare	Occasional
Pain relief	Standing	Flexion and sitting
Posture provocation	Uncommon	Common
Walk up hill	Pain	No pain
Bicycle riding	Pain	No pain
Pulses	Absent	Normal
Trophic changes	Likely	Absent
Muscle atrophy	Rare	Occasional

1.10. CLASSIFICATION OF LSS

Lumbar spinal stenosis may be classified by either its aetiology or location. The classification of lumbar stenosis is important because of the implications of the underlying aetiology of the condition and when forming a therapeutic strategy, specifically directing surgical approaches.(60)

1.10.1. Aetiological classification

According to Arnoldi et al,(61) aetiological classification comprises two major groups: primary (congenital or developmental stenosis) and acquired stenosis. Primary stenosis is caused by congenital narrowing of the spinal canal. (23)(24)(62)

Congenital stenosis is divided additionally into idiopathic and achondroplastic aetiologies. Acquired (secondary) stenosis can result from a wide range of conditions, most often chronic degeneration, which leads to a destabilized vertebral body. Acquired stenosis is subclassified into degenerative, combined congenital and degenerative, spondylotic and spondylolisthetic, iatrogenic posttraumatic, and metabolic (Table 1.2.). Other causes of secondary stenosis include rheumatoid diseases, osteomyelitis, trauma, tumours, and, in rare cases, Cushing disease or iatrogenic cortisone application.(62)

1.10.2. Anatomical classification

Anatomical classification incorporates central canal stenosis, lateral recess stenosis and neural foraminal stenosis (Table 1.2.).

TABLE 1. 2. Classification of Spinal Stenosis (*63)*

Aetiological classification
Congenital (primary or developmental stenosis)
Idiopathic
Achondroplastic
Acquired stenosis – much more common
Degenerative
Congenital or degenerative
Spondylotic or spondylolisthetic
Iatrogenic (postlaminectomy, postfusion)
Posttraumatic
Metabolic (Pagets disease)
Anatomical classification
Central canal stenosis
Lateral recess stenosis
Neural foraminal stenosis

1.11. INVESTIGATIONS

1.11.1. Imaging

There are a few inherent problems with imaging of the lumbar spinal canal that need to be considered.

First, degenerative changes in the lumbar spine are very common in the asymptomatic population, especially in patients over 60 years of age, 20% will reveal signs of LSS.(64). This confounds imaging of symptomatic patients.

Second, it has been shown that imaging often tends to exaggerate pronounced degenerative changes and effects on the spinal canal.(62)(65) Imaging tends to be used most frequently in patients with medium to severe symptoms of LSS. (66)

The purpose of imaging is to assess the extent of LSS, to rule out other differential diagnoses, and to point out the pathological anatomy of LSS for the purpose of preoperative planning.(62)(67)

In LSS, imaging studies include:

1.11.1.1. **Plain radiographs of lumbar spine:-** Routine use of plain radiographs when evaluating patients with LSS has been questioned.(62)(68)(69) Conventional radiographs might be of use, albeit in a limited fashion, in assessing the contribution of bony degeneration to LSS and the alignment of the vertebral bodies in lateral and coronal planes. It can also potentially be used to rule out traumatic changes or other findings (e.g. Paget disease, spondylolisthesis or scoliosis) as possible differential diagnoses.(62)(70) The sensitivity and specificity of plain radiographs concerning the contribution of bony changes to central spinal stenosis were reported to amount to 66% and 98% respectively of those of CT. The need of additional lateral radiographs in flexion and extension to rule out segmental instability is not routinely required, as segmental instability can be detected on routine lateral radiographs in a reasonably accurate manner.(62)(71) It is shown that no additional benefits were conferred from these additional views (62)(70) Interestingly, even in patients for whom segmental instability was expected,

the diagnostic purpose of lateral radiographs in flexion and extension views, is not definitively determined.(62)(72)

1.11.1.2. **Magnetic resonance imaging (MRI) of lumbar spine**: - MRI is the preferred imaging modality for the radiological assessment of LSS. (73). This technique provides superior soft tissue contrast compared with other imaging modalities, has multiplanar imaging capabilities and does not produce ionizing radiation. MRI is contraindicated in patients with pacemakers, certain other types of metal implants or claustrophobia.
MRI of patients with LSS usually comprises T1 weighted and T2 weighted images (sagittal and axial). A fat-suppressed T2 weighted sequence can be added, as such images seem to allow more accurate detection of associated degenerative bone marrow changes. With T2 sequences and with signal intensity of cerebrospinal fluid, images of the thecal sac, the intrathecal and intraforaminal nerve roots, and the spinal cord can be obtained noninvasively. MRI can also visualise the bony and discoligamentous structures contributing to LSS, similar to the computed tomography imaging. Interestingly, some studies have produced conflicting results concerning the clinical usefulness of the information gained by MRI.(62)(74)(75)
It has been implied that changes observed by means of MRI add little clinically useful information to clinical assessment alone in relation to prognosis and predicting the outcome of surgery. (74)(76)
Contrast-enhanced MRIs are only required if previous surgery was done and fibrous scar need to be excluded. (77)(78).
Other studies have suggested that contrast-enhanced MRI in LSS patients with neurogenic claudication can help in viewing the enhancement of compressed nerve roots which can be visualized in some patients. (79)(80)(81)
This enhancement is thought to reflect either obstructed peri-radicular veins, indicating venous stasis, or breakdown of the blood–nerve barrier, a sign of chronic compressive radiculitis.

1.11.1.3. **Computed tomography (CT):** -CT of lumbar spine is helpful to visualize the bony and discoligamentous anatomy. It has also an additional purpose of ruling out any compression fractures and assessing previous surgery or instrumentation. It can be performed rapidly and allows differentiation between spinal canal compression caused by discs, ligaments and bony structures.

A limitation of CT is that intrathecal nerve roots and the spinal cord cannot be visualized, because these structures have similar densities to the cerebrospinal fluid.

1.11.1.4. **CT myelogram:** - At present, this is the only accurate imaging technique for patients with spinal metallic implants, which can cause artefacts on MRI and CT. It is an invasive procedure that requires intrathecal administration of iodinated contrast agent. Consequently is associated with side effects such as post-lumbar puncture headaches, anaphylaxis and spinal infections. Like other imaging techniques, conventional myelography frequently reveals abnormalities that were not suspected clinically.(65)

However, there are studies that have shown that the diagnostic and predictive values of conventional myelography, CT myelography and MRI are not markedly different.(82)

1.11.2. **<u>Correlation of clinical features with radiological findings</u>**

It has been shown that the radiological degree of LSS, both before and after surgery, does not necessarily correlate with the degree of the clinical signs and symptoms. (47)(64)(82)(83)(84)

As previously mentioned, it has been shown that imaging often tends to exaggerate pronounced degenerative changes and effects on the spinal canal. (65).

Thus, radiologically diagnosed LSS usually identifies involvement of more segments than is suspected clinically (66)

The aim of imaging is to assess radiologically the extent of LSS, to rule out differential diagnoses, to relate stenotic symptoms to osseous and

discoligamentous structures, and to identify the exact location of LSS for preoperative planning.(67)

1.11.3. Additional diagnostics

1.11.3.1. **Pain injections:** - Selective pain injections can be useful to estimate the contribution of different pain components to the symptoms of the LSS.

1.11.3.2. **Nerve conduction studies:**

Given the low practical importance of classical electromyography and nerve conduction studies in diagnosing LSS, an electrophysiological examination is only recommended to exclude other disorders, especially if the distribution of pain and numbness is unusual (for example, suspicion of peripheral polyneuropathy or myopathy, which might both occur concomitantly with LSS). (83)(84)

1.11.3.3. **Walking treadmill test:**

Walking on a treadmill is an appropriate provocation test for the assessment of extent of LSS, although this technique is not yet common in daily practice. (83)(84).

1.11.3.4. **Routine laboratory tests**:

This tests can be used to detect comorbidities, such as diabetes or diabetic polyneuropathy (by detection of glucose and Hba1c), and infections such as spondylodiscitis (by measurement of C - reactive protein). (62)

1.12. **TREATMENT**

Decision-making regarding treatment of LSS is a complex issue considering the progressive nature and the heterogeneity of the condition. Treatment strategies have mostly focused on pain and physical function as primary end points.(47) Because of the lack of therapeutic recommendations and the large number of distinct therapies, the selection of an appropriate procedure is difficult.(13) The need for prospective, randomized studies comparing the various therapies are required.(48)(6)

The treatment for LSS can be: conservative (nonoperative) and operative.

The standard operative treatment for lumbar stenosis includes decompressive laminectomy and/or foraminotomy at appropriate levels. As most patients are elderly, they can have multiple medical comorbidities including cardiac, pulmonary, or renal disease. For this reason, less invasive surgical treatments have been sought, including minimally invasive approaches and interspinous spacers. More recently, preservation technologies, such as the X-stop device, Wallis Normalization System, or Device for Intervertebral Assisted Motion (DIAM), have been developed and used.

1.12.1. CONSERVATIVE MANAGEMENT:

1.12.1.1. Overview

Typical nonoperative management of lumbar stenosis includes:

- physical therapy,
- nonsteroidal anti-inflammatory drugs,
- braces, or
- epidural steroid injections.

The effectiveness of conservative therapy in treating LSS has been reported to have high success rates.(85)(86)(87) In one study there was 70% clinical improvement compared to baseline when non-surgical treatment by physiotherapy was applied. This study included 57 patients with LSS and follow up over 3 years. Limitations of this study were small sample size, with 25% of these patients who did not have MRI lumbar spine. Those with radiologically confirmed LSS had various levels of lumbar spine affected. Also three patients with previous lumbar surgery were included in the study.(85)

However, none of the studies has provided a full support for a single conservative treatments. (4)(88)

In the absence of clear evidence-based guidelines, it has been suggested that a multidisciplinary approach should be given preference over a single therapy.(88)(89)

The main objectives of physiotherapy are flexion, distraction, neural mobilization, relief of the affected segments and improvements in paravertebral muscle tone with stabilizing exercises. (85)

There is a consensus between clinicians that bed rest is not recommended in the therapy of chronic and acute pain.(88)

The pharmacological component of conservative therapy aims to relieve painful nerve root pathologies. Drugs used to treat LSS include NSAIDs, other peripheral analgesics, steroids, muscle relaxants, opioids, antidepressants and, in very severe cases, neuroleptics.

Evidence-based facts mainly suggest short-term efficacy of administration of NSAIDs, muscle relaxants, steroids, antidepressants and opioids. (4)(89)

Likewise, the evidence for the efficacy of therapeutic injections for LSS has not been confirmed. (90)(91)

1.12.1.2. Evidence of outcomes of conservative vs surgical management

Numerous studies have been performed to compare nonoperative and operative approaches to the spondylotic spine.

There are RCTs that assessed surgical versus conservative approaches. In one trial, 44 patients with mild-to-moderate leg pain were randomized to receive conservative treatment (i.e., back braces, physical therapy, and exercise programs) or lumbar laminectomy. Both treatment groups showed significant clinical improvement after 1 year of treatment. However, only the surgery group continued to show improvement after 2 years.(92)

In the second trial, patients with moderate pain were randomized to undergo surgery or receive conservative therapy again (i.e., bracing and physical therapy).(65)

Patients with more severe pain underwent surgery, and patients with milder symptoms received conservative therapy. Within 3 to 27 months of starting the study, 10 out of the 18 (56%) conservatively treated patients with moderate

symptoms crossed over to the surgery group. Among patients with moderate symptoms, a greater proportion of surgery patients had a decrease in symptoms. These data further suggest that surgery may be more beneficial than conservative therapy in patients with moderate to more severe symptoms.(93)

The randomized controlled trial (94) looked at operative versus nonoperative treatment for lumbar spinal stenosis. This Finnish study aimed to assess the efficacy of decompressive surgery in comparison with conservative treatments such as nonsteroidal anti inflammatories and routine physical therapy. A total of 94 patients were randomized, 50 to the operative arm and 44 to the conservative treatment arm. The operative arm received a decompressive laminectomy at the stenotic levels and in 10 of these patients, an instrumented fusion was performed with pedicle screws.

In the same study (94), there was an improvement in the functional disability score and pain scores for both groups. However, the surgical arm was found to benefit more with regard to back and leg pain, and overall disability. This study confirmed that there is a place for conservative management of lumbar spinal stenosis; however, surgery seems to be more effective, especially during the first year. Outcomes remained favourable at 2 years, however. longer follow-up is needed in these patient arms to get a better feel for long-term differences between the nonoperative and operative arms.

The Maine Lumbar Spine Study was a prospective, observational cohort study, with a subgroup of patients with moderate neurogenic claudication. The follow up for this study was over an 8 to 10-year interval. 56 underwent surgery, and 41 were treated with conservative management to include bed rest, physical therapy, exercise, braces, traction, transcutaneous electrical nerve stimulation, spinal manipulation, narcotic analgesics, or epidural steroids.(95)

After 8 to 10 years, of the 62% of patients who chose to forego surgical intervention had no worsening of their symptoms. Thus, the remainder, or 38%, of these patients actually crossed-over to the surgical arm. The authors concluded that, with time, it was likely symptoms of lumbar spinal stenosis would remain stable for many patients who had surgery. Unfortunately, the same study found diminished benefits (despite initially better baseline symptoms) in those patients who elected to wait before crossing over to the surgical side.(95)(96)(97)

Notably although, at 10 years, patients who had been treated surgically reported less leg pain and greater improvement in functional status than the nonoperative patients.

Another study known as the Spine Patient Outcome Research Trial (SPORT) reported 2-year outcomes of patients with spinal stenosis with regard to operative versus conservative therapies.(98) This study looked at 289 patients as a randomized cohort and 365 patients as an observational cohort. These patients had 12 weeks of symptomatic spinal stenosis without spondylolisthesis. Surgical treatment consisted of decompression with only 6% receiving instrumented fusion. The nonsurgical treatment consisted of medical therapy including steroid injections.

This study found that surgery was superior to nonsurgical therapy in improving patients' symptoms and improving function. However, results were affected by significant lack of adherence to treatment assignments by randomization.

1.12.1.3. Epidural steroid injections

The mechanism of action of epidural injections is thought to consist of neural blockade altering or stopping nociceptive input, reflex mechanisms of the afferent limb, self-sustaining activity of the neuron pools and neuroaxis, and the pattern of central neuronal activities.(97) It has been demonstrated that all lumbar epidural steroid injections provided short-term relief but limited long-term relief.(97)

One randomized placebo-controlled trial studied the effects of epidural steroid injections and a local anaesthetic on neurogenic claudication.(99)

This study suggested that the local anaesthetic mepivacaine would reduce symptoms while increasing walking distance in the short-term. However, these effects last for no more than 1 month. Epidural steroids seemed to offer no additional benefit to the effects of the anaesthetic block, however. In patients with more severe symptoms who have failed conservative management, surgery was thought to be more beneficial.

Caudal epidural steroid injections are commonly used to help reduce radicular pain in lumbar spinal stenosis. In a study, the therapeutic benefit of fluoroscopically guided caudal epidural steroid injections was evaluated in the treatment of bilateral radicular pain from symptomatic lumbar spinal stenosis.

This prospective cohort study was performed on 34 patients with bilateral radicular pain from lumbar spinal stenosis who received epidural injections as they did not improve with other therapy. Patients were injected once, and then again at 6 weeks, 6 months, and 12 months after the injections. 65% of patients at 6 weeks, 62% at 6 months, and 54% at 12 months had a successful outcome, reporting at least a 50% reduction between pre-injection and post-injection visual analogue scores. Fifty-nine percent of patients had an improved walking tolerance at 6 weeks, 56% at 6 months, and 51% at 12 months.(100)
Another retrospective study,(101) looked at the duration and amount of pain relief, change in functional status, patient satisfaction, and surgical rate. The researchers found that 39% of patients reported less than 2 months of pain relief, 32% more than 2 months, and 29% reported no relief from the injections. Twenty percent subsequently had surgery. They concluded that epidural steroid injections are a reasonable treatment for lumbar spine stenosis, providing for some pain relief and some sustained improvement in function as well.

1.12.1.4. Physiotherapy

In a RCT 58 patients with LSS were randomized to one of two 6-week physical therapy programs. One program included manual physical therapy, body weight supported treadmill walking, and exercise, whereas the other included lumbar flexion exercises, a treadmill walking program, and subtherapeutic ultrasound. A greater proportion of patients in the manual physical therapy, exercise, and walking group reported recovery at 6 weeks compared with the flexion exercise and walking group. At 1 year, 62% and 41% of the manual therapy, exercise, and walking group and the flexion exercise and walking group, respectively, still met the threshold for recovery. Thus, it seems that patients with lumbar spinal stenosis can benefit from physical therapy.(102)

1.12.2. OPERATIVE MANAGEMENT

Patients with established diagnosis of LSS from clinical history, physical examination and radiological assessment, would usually have conservative treatment applied for 3–6 months. If severe symptoms persist and functional impairment develops, surgery is the recommended option, unless there are contraindications or patients are unwilling to undergo the operation. Some patients may have unrealistic expectations of what can be achieved with surgical procedures. (103)

The aim of the procedures in LSS is to decompress the entrapped neural elements, without disrupting the stability of the segment. Such decompression surgery usually leads to spontaneous relief of pain in the legs, and, to a lesser degree, of low back pain. (95)

The speed and extent of recovery is, however, unpredictable, even if pressure on nerve roots, dura and blood vessels is sufficiently eliminated. Decompressive surgical procedures include laminectomy and hemilaminectomy, hemilaminotomy, fenestration, foraminotomy and the implantation of interspinous distraction devices.(91)(104)(105)

1.12.2.1. Lumbar laminectomy

Lumbar laminectomy is a common operation and involves removal of the lamina of the symptomatic stenosed spinal levels.

Early treatment is important for a successful outcome in those who are deemed surgical candidates. Surgical decompression of the neural structures usually treats the symptoms effectively and patients often can resume some active lives compared to preoperative states.(106)

Importantly, patient selection is key.(107) The history, physical examination, and appropriate imaging studies provide enough information to make the correct diagnosis. Some patients may require further studies, such as somatosensory evoked potentials, electromyography, vascular tests, including an ankle brachial index, or lumbosacral plexus imaging, to confirm the diagnosis.

The selection of more severe cases of LSS for surgery and less severe cases for conservative treatment, has potentially introduced a major selection bias in all retrospective and prospective non-randomised trials. This has made difficult the decision-making process in choice between conservative therapy and surgery.(108)

Cochrane reviews of surgical treatments for spinal stenosis concluded that there is still insufficient evidence to support surgery over nonsurgical treatments.(4)(109)

A pair-matched study demonstrated no statistically significant difference in clinical outcome between surgically decompressed and conservatively treated patients after a 4year follow-up period. (110)

In a further study 5–10 years after treatment there was no longer a significant difference between the two groups with regard to back pain and patient satisfaction with their condition, although differences in leg pain and functional status were still detectable. (108)

Two prospective trials indicated that surgical decompression is superior to conservative therapy. (47)(111) However, the differences in pain relief and improvement in functional status narrowed during the 2 year follow-up period (47).

Aside from the short period to follow-up, other limitations of the study were the use of only one type of operation and the high rate of crossover from surgery to conservative therapy and vice versa. Moreover, a later meta-analysis was unable to provide evidence for the effectiveness of surgery in patients with LSS. (89)

So far, only a few prognostic signs, such as young age, (112) short preoperative duration of claudication (the absence of sphincter dysfunction and atrophy), symptom relief with lumbar flexion and a limited number or absence of comorbidities (for example, peripheral vascular disease and cardio-vascular disorders), predict a favourable outcome after surgery.(113)(114)(115)

In addition, in the case of concomitant degenerative spondylolisthesis, the clinical results are better after surgery than after conservative therapy. (116).

The extent of radiological findings are generally of little help for the identification of a surgery indication.

1.12.2.1.1. Success rate: - Success rates for decompression surgery in cases of LSS range from 40–90% in the literature and depend on a wide variety of factors such as type of decompression, duration of follow-up, age of patients and comorbidities. (60) (113) (117) (118) (119) (120) (121)

1.12.2.1.2. Complication rate:- The complication rates for decompression surgery (during and after the surgical procedure) range from 14% (116) to 35% or more.(122) (123)

1.12.2.2. Interspinous spacers

New techniques for the treatment of lumbar stenosis include motion preservation devices known as interspinous distracters (Figure 1.2). Examples of such devices include the X-stop device, the Wallis System, the DIAM, and the Coflex system. As the name implies, the mechanism by which these devises work, is by providing distraction between the spinous processes hence providing extra space to the neural foramina and lateral recesses.

The X-stop interspinous distraction device has shown to be an attractive alternative to conventional surgical procedures in the treatment of symptomatic degenerative lumbar spinal stenosis.

1.12.2.2.1. **Biomechanics**

The understanding of biomechanics of interspinous distracters is important to understand their therapeutic role in treatment of LSS.

In vitro studies in cadaveric spinal column specimens have shown that IPDs have following biomechanical effects:

- IPDs do not change:
  - the ROM in flexion, extension, lateral rotation and axial rotation.
  - the intradiscal pressure in flexion, lateral rotation and axial rotation.
- IPDs reduce:
  - the intradiscal pressure in extension

  (124)

There is cadaveric evidence that X-stop reduces flexion-extension range at the instrumented level with no effect on axial rotation and lateral bending ranges of motion. The range of motion in flexion–extension, axial rotation, and lateral bending at the adjacent segments was not significantly affected by the implant.(125)

Another study has shown that in extension, the implant significantly increased the spinal canal area by 18% (231–273 mm2), foraminal area by 25% (106–133 mm2), and the foraminal width by 41% (3.4 – 4.8 mm).(126)

In addition, another study has shown that the pressures at the adjacent discs were not significantly affected by the interspinous implant insertion.(127)

These findings could explain the proposed mechanism of beneficial effect of the X-stop device.

1.13. **Clinical outcomes**

Numerous studies have shown the superiority of operative treatment compared to conservative treatment for LSS patients.

The first RCT comparing the clinical efficacy of X-stop versus conservative treatment showed the success rate of 52% for X-stop patients and 10% for conservatively managed patients at 6 weeks. At 6 months, the success rates were 52 and 9%, respectively, and at 1 year, 59 and 12%. The results of this prospective study indicate that the X-STOP offers a significant improvement over non-operative

therapies at 1 year with a success rate comparable to published reports for decompressive laminectomy, but with considerably lower morbidity.(128)
Using the ODI and a clinical exam as the outcome measures, the authors did not find a significant difference in subjective disability or functional status between the two groups.(129) (130)
At 2 years follow up of the same study, the X-stop patients improved by 45.4% over the mean baseline Symptom Severity score compared with 7.4% in the control group; the mean improvement in the Physical Function domain was 44.3% in the X-stop group and 0.4% in the control group. In the X-stop group, 73.1% patients were satisfied with their treatment compared with 35.9% of control patients. The X-stop provides a conservative yet effective treatment for patients suffering from lumbar spinal stenosis. In the continuum of treatment options, the X-stop offers an attractive alternative to both conservative care and decompressive surgery such as lumbar laminectomy.(131)
Same study, followed up 18 patients who have had X-stop and suggested that X-stop success is stable as measured by ODI. ODI showed that the success rate in the X-stop interspinous process decompression group was 78% at an average of 4.2 years postoperatively. The results suggest that intermediate–term outcomes of X-stop surgery are stable over time as measured by the ODI.
Limitations of the study are a high rate of loss to follow up, small sample size and no indication that statistical testing was performed considering that there were no patients in conservative treatment to be compared with. (132)
The significant clinical outcomes of the X-stop were also shown by other studies. (133)
In a similar manner, two major RCTs showed that lumbar laminectomy demonstrated significantly improved outcomes compared to conservative treatment.(98) (111)

1.14. Quality of life

At the 6-week, 6-month, and 1-year post-treatment follow-up time points, the X-stop group scored significantly better than the non-operative group in every domain. In addition, at each time point, the mean scores in each category for the X-stop group were significantly better than the respective pre-treatment scores, whereas in the non-operative group, none of the mean scores was significantly better.(128)

It has been suggested that SF-36 domain scores are valid for measuring morbidity and surgical outcomes in common spinal disorders. (134)

It was shown that the EQ-5D is useful for estimating health state values and for monitoring outcome of patients undergoing low-back surgery. Hence, this instrument would provide valid data for cost– utility analyses in lower back surgery.(135)

Another study showed an improvement in EQ5D postoperatively following lumbar laminectomy operation.(136)

The long-term follow-up showed that patients operated on for LS continue to improve their QoL pattern even between the 4th and the 8th year after surgery. Specifically improvements were observed in Physical Function, Bodily Pain, Mental Health and the Physical Composite Score with respect to the first follow-up. Conversely, Vitality worsened during this follow up.(137)

1.15. Radiological parameters

The biomechanical effect of X-stop on the vertebral spine has been used to explain the beneficial effect of the implant. It has been shown that X-stop significantly increases the foraminal height, foraminal width, foraminal cross-sectional area, intervertebral angle and decrease in anterior disc height and posterior disc height.(138)

The widening effect on spinal canal area and neural foramina was confirmed in another study.(139) (140)

1.16. Costs associated with operations

There are two studies supporting the use of X-stop over lumbar laminectomy on the grounds of higher cost-effectiveness.(141) (142)

Although both studies were RCTs both studies only chose a subgroup of laminectomy patients and as such introducing some selection bias.

1.17. Economical evaluation of health

Excellent description of health economic evaluation is given in book by Morris et al, 2007. (143)

In view of current financial climate and limited budgets, understanding the health economics is becoming increasingly important concerning the decision-making in provision of care.

Two main factors underpin the economic analysis:

- resources are limited, and
- potential uses of those resources are unbounded.

1.17.1. Cost-benefit analysis(CBA)

CBA is the analysis of decision regarding whether to do or not to do something, which depends on weighing its costs and benefits.

1.17.2. Cost-effectiveness analysis (CEA)

The special case of CBA is the *cost-effectiveness analysis* (CEA), which seeks to answer the question of which among the two or more alternatives provides the most output for a given cost, or the lowest cost for a given output. To compare alternatives, cost –effectiveness ratio (CER) is used, which is calculated as a cost per unit of output or effect.

The health measure used to calculate CER is gains in quality adjusted life years (QALYs). QALY is a composite measure of gains in life expectancy and health-related quality of life.

1.17.3. **Cost-effectiveness ratio (CER)**

Let us assume that Ca and Cb are the costs of the standard treatment a and its best alternative b respectively. Also, let us assume that Ea and Eb are the effects health measures of the standard treatment a and its best alternative b. Then the CER is calculated as follows:

$$\text{CER} = \frac{(Ca - Cb)}{(Ea - Eb)}$$

or

$$\text{CER} = \frac{\Delta C}{\Delta E},$$

where,

Incremental cost = ΔC = Ca – Cb; Incremental effect = ΔE = Ea –Eb

1.17.4. **The Cost-Effectiveness Plane**

The cost-effectiveness plane is a useful way of showing the decision rules that apply to the CER. (144)

In the diagram (Figure 1.3) the vertical axis represents the difference Incremental cost ΔC diagram while the horizontal axis shows the Incremental effect ΔE of an activity compared to some alternative. These lines divide all possible cost and effect combinations into four quadrants. The CER in north-west quadrant indicate that costs are higher and effects are lower. Therefore, the activity is said to be dominated by its alternative and should not be used. On the other side, to the south-east, costs are lower and the effects are greater, so the activity dominates its alternative and should be used. In the other two quadrants, either greater effectiveness is gained at a higher cost (north-east quadrant), or a reduction in costs is achieved at the expense of lower effects (south-west quadrant). In these two quadrants, whether or not the activity should be undertaken on the efficiency grounds depends on the trade-off between costs and effects.

The slope of a line from the origin represents the CER of an activity.

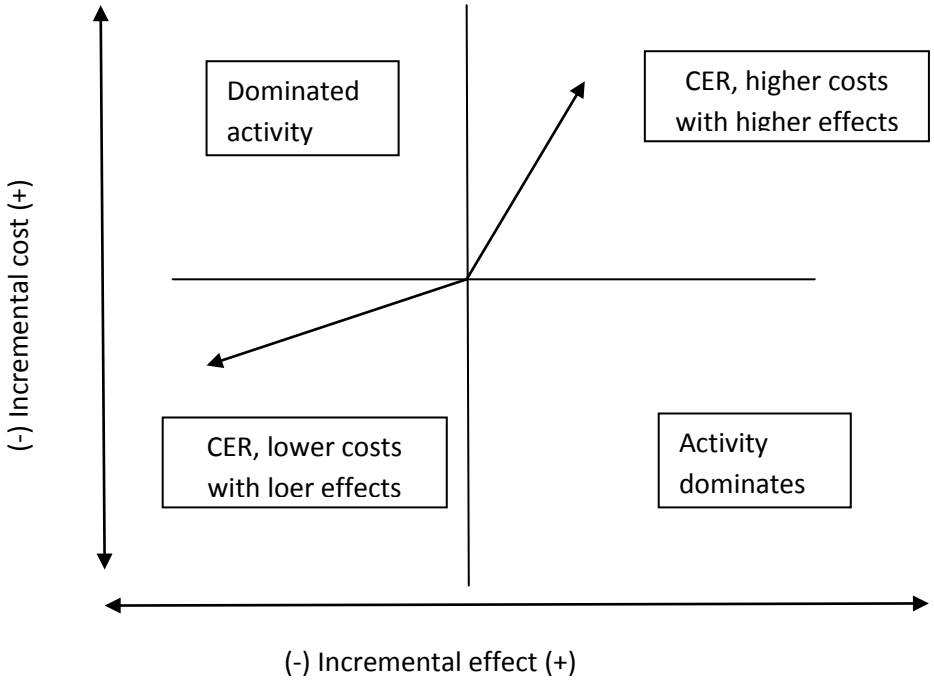


Figure 1.2: The cost-effectiveness plane

1.17.5. The Incremental Cost-Effectiveness Ratio (ICER)

The ICER refers to comparing the activity with another alternative i.e. 'another way of doing something'. There is one precondition which requires that the alternative is cost-effective itself otherwise the results may be misleading (e.g. non-cost effective alternative which when used in comparison with the alternative spuriously seems to be cost-effective).

1.17.6. Measurement of health outcomes

There are two types of questionnaires used: disease-specific and general questionnaires used to get the health outcome measures. Disease-specific questionnaires, as the name suggests, attempts to address functional status of the patient regarding the particular disease. The general questionnaires measures health outcomes by its impact on quality of life (QOL) or health-related QOL (HRQOL).

The HRQOL is defined as:

'The value assigned to duration of life as modified by the impairments, functional status, perceptions and social opportunities that are influenced by disease, injury, treatment or policy.'(145)

Questionnaires which measure the HRQOL indicators are called *instruments*. The people who are completing the questionnaires are called *respondents*.

1.17.7. Criteria's for health outcome questionnaires

The principal criteria for a good health outcome questionnaire are:

- reliability –produces consistent measurements
- validity – measures what is supposed to measure
- responsiveness – it means how sensitive the results from the health outcome instrument are to changes in health. If people who have a serious illness have the same HRQOL scores as healthy people, we might suspect that the instrument is not very sensitive.
- feasibility – how acceptable is instrument to the respondents i.e. relevance or length issues.

1.17.8. Types of health outcome measures

There are two types of health outcome questionnaires:

1. *Generic health state instruments* – (such as EQ5D and SF36) intended to be independent of particular health conditions and interventions and therefore applicable in all circumstances. These measures are intended to be all-encompassing measure that tells you all you need to know in every circumstance, and sometimes a common minimum data set collection is collected for various facets of health (e.g. pain, dysfunction, mobility, washing, dressing etc).
2. *Disease-specific (or treatment- or domain-specific) health questionnaires* – (such as Zurich Claudication Questionnaires) intended only for a specific illness (or treatment- or domain-specific health state).

1.17.9. **Measurement of health gain**

The health gain is calculated as a difference with and without the intervention. This health is regarded as the product of the level of health and the length of time experienced (Figure 1.4.).

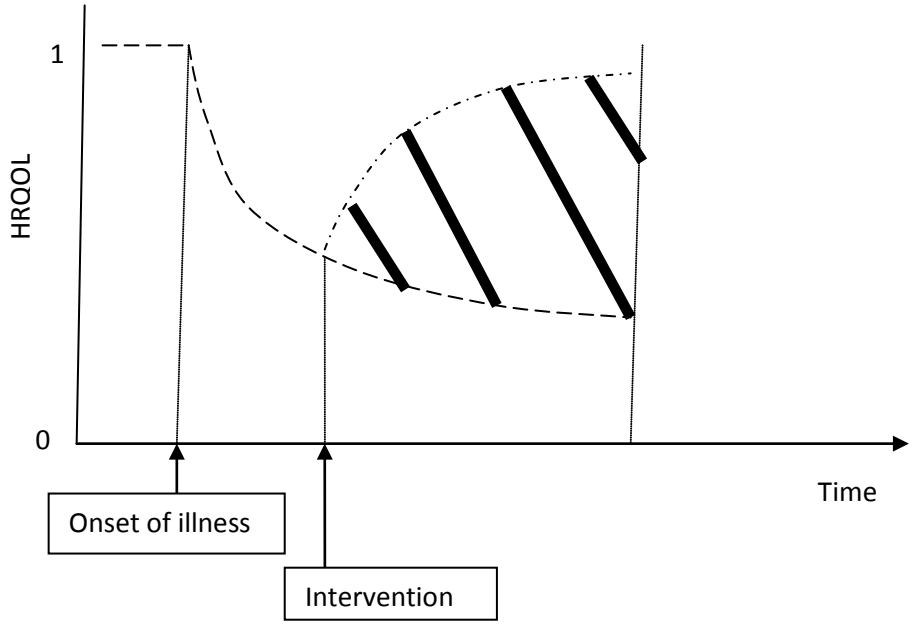


Figure 1.3: Measuring the health gain (area shown by the diagonal shading) from intervention. (143)

The most common measure used is quality-adjusted life years (QALYs). QALYs are calculated similarly as the example above, by multiplying the amount of time in a particular health state by the quality of life during that time, then summing up over all time periods.

1.17.10. **Thresholds in cost effectiveness analysis**

What represents society's willingness to pay for a unit of health improvement? In the UK, the threshold value of CER proposed by NICE is considered as £30000/QALY.

It has been stated that:

‘NICE would be unlikely to reject a technology with a ratio in the range of £5000 - £15000/QALY solely on the ground of cost-ineffectiveness but would need special reasons for accepting technologies with ratios over £2500 - £35000/QALY as cost effective.’(146)

The so-called cost-effectiveness acceptability curve showing the probability that the standard treatment is more cost effective for various maximum acceptability ceiling ratios (thresholds).(147)

1.17.11. Cost-effectiveness versus Clinical evidence in decision making

So the question arises of where do we stand when we have the cost-effectiveness evidence and clinical evidence regarding the standard treatment and its alternative.

Cost-effectiveness evidence seems to explain decisions to recommend for or against a therapy, whereas clinical evidence considers the decisions to recommend restricted or unrestricted use.(148)

2. BACKGROUND TO THE STUDY

Lumbar spinal stenosis (LSS) is a common and debilitating condition, which consumes large amounts of healthcare resources. It occurs in 13-14% of patients who consult a specialist with back-pain, and in the US costs tens of billions of dollars in health-care.(125)

Degenerative changes in the facet joints and ligamentum flavum cause narrowing of the spinal canal and compression of lumbar nerve roots. This results in neurogenic claudication: a debilitating pain or heaviness in the legs that is aggravated by walking, thereby limiting mobility. There have been an increasing number of treatments for LSS over the years, including physiotherapy, lumbar laminectomy, lumbar foraminotomy and devices for interspinous distraction. Lumbar laminectomy and interspinous distraction are both effective methods for treatment of LSS but there is little published

regarding the cost effectiveness of these treatments and quality of life for patients.

Lumbar laminectomy is a relatively safe operation, but it is thought that it results in longer operative time, more immediate post-operative back-pain, longer hospital stay, and greater complications compared to the insertion of the X-stop device. However, the cost of the X-stop device itself has to be weighed against the advantages. This constitutes the basis for this study.

The all Titanium X-stop device was first implanted nearly 15 years ago as part of a series of developments of the evolving product. The current Titanium versions gained CE mark approval in 2002 and the Titanium plus PEEK upgrade (XSTOP$^{PK®}$) shortly after that. In the USA, a multicentre randomised controlled trial (RCT) was conducted comparing X-stop surgery to conservative therapy in a population of patients with Lumbar Spinal Stenosis (135) The RCT results were submitted to the FDA in a full PMA application, and FDA approval to market the XSTOP® was granted in November 2005.

The current biomechanical model suggests that placement of the XSTOP$^{PK®}$ implant in the anterior column will result in load sharing and thus reduced strain on degenerative lumbar discs with concordant pain relief.

This prospective, randomised, multi-centre study seeks to show that X-stop device despite the extra cost of the implant itself, is more cost effective. This presumed cost effectiveness is linked to presumed shorter operative times, lower risk of dural damage associated with surgical decompression techniques and the associated costs of treating this problem, shorter hospital stays, potential use of local anaesthesia for the procedure and faster rehabilitation. We have undertaken the task of prospectively and in a randomised fashion, to compare the cost effectiveness, clinical outcomes and safety of X-stop versus surgical decompression in the treatment of symptomatic lumbar spinal stenosis. Effectiveness of the different treatments will be assessed using general quality of life questionnaires and disease-specific questionnaires.

2.1. *Primary end-point*

Primary end-point of our study is to assess the cost-effectiveness of lumbar laminectomy versus X-stop device insertion.

2.2. *Secondary-end points*

Secondary end-points to the study are comparing between and within each treatment group the following:

- Quality of life as measured by:

- EQ5D and VAS

- SF36 and separately for each domain.

- Costs

- Clinical outcomes:

- Quebeck Back Pain Disability Score

- Oswestry Disability Index,

- Zurich Claudication Questionnaire

- Assessing predictive factors for:

- Quality of life,
- Costs
- Clinical outcomes

  Ten predictive factors considered are: ASA score, age, smoking status, gender, duration of symptoms, actual levels operated, number of levels operated, BMI, procedure (Lumbar laminectomy versus X-stop), and Cobb angle.

- Correlation between general quality of life and disease-specific questionnaires as applied to lumbar stenosis patients. The aim here is to work out if there is a significant valid convergence for the use of EQ5D and SF36 in lumbar spinal stenosis patients.

- Assessment of radiological changes associated with each intervention.

- at the same level
- if there is any evidence of accelerated degeneration

  Radiological parameters analysed are: - spinal canal area, foraminal area, fact joint size, anterior disc height, posterior disc height, Cobb angle, intervertebral angles. Also, the upper and lower adjacent vertebral levels to the operated level(s) were assessed for changes in: -spinal canal area, foraminal areas, facet size, ligamentum flavum, disc heights.

- Complications

- Reoperation rates.

- Sample size calculations –as derived from this pilot study

3. METHODS

3.1. Study design

The purpose of this thesis is to inform a larger UK based prospective, randomised multi-centre study, by providing pilot data of sample size, feasibility and outcome. The Ethics approval was obtained from the National Research Ethics Committee UK and the study is registered with International Standard Randomised Controlled Trial (ISRCTN88702314).

Recruitment was done from two UK neurosurgical centres. Patients are initially assessed against our inclusion and exclusion criteria (see below). After reading Patient Information Sheet eligible patients were recruited into the study after giving written informed consent and they were subsequently subject to the routine surgical and post-operative care at each participating centre.

Assessments have been carried out similar to the routine practice with strict appointments at the following time periods: preoperatively; intraoperatively and postoperatively at discharge, 6 weeks, 6, 12, 24 months.

This thesis constitutes the analysis of the first 12 months following the randomisation and operation.

3.2. Primary Objective

The primary objective of this clinical investigation is to provide pilot data of whether there is a difference in cost of implanting XSTOP® *PK* compared to conventional surgical decompression, initially at 2 weeks post-op and up to 12 months.

3.3. Secondary Objectives

The secondary objectives are to compare quality of life measures between the two groups (EQ5D, SF-36), clinical efficacy (QBPDS, Oswestry disability index, Zurich Claudication Questionnaire), radiological parameters and complications.

3.4. Patient Selection

3.4.1. Randomisation and Blinding

In order to ensure similar numbers of treatment allocation between the two groups, balanced block randomisation was done of size ten with 1:1 treatment allocation ratio in each block. The random allocation was obtained via computer random number generator. An independent person not involved in the study did the random number assignment and preparation of identically looking envelopes. After eligibility had been confirmed, patients were randomly assigned by selection of the concealed lowest numbered treatment envelope from each block batch.

Randomisation envelopes were opened on the day prior to surgery, to facilitate theatre planning, and the appropriate procedure completed.

3.4.2. Target Population

Patients with at least 6 months unsuccessful conservative treatment for Lumbar Spinal Stenosis with Neurogenic Claudication with/without lower back pain (LBP) were considered for inclusion in this study. There should be no evidence of psychiatric disease or ongoing litigation, and all patients should be considered suitable for posterior or postero-lateral lumbar spine surgery for the treatment of their condition.

Patients who fulfil the following inclusion and exclusion criteria were considered eligible to be entered into this investigation.

3.4.3. Inclusion Criteria

Patients were admitted in the study if they met all of the following inclusion criteria:

a) is a male or non pregnant female patients

b) is aged between 18-80 years (inclusive)

c) has a BMI <35 kg/m^2

d) has chronic leg pain with or without back pain of greater than 6 months duration, partially or completely relieved by adopting flexed posture and who are suitable candidates for posterior lumbar surgery

e) has completed at least 6 months of conservative treatment without obtaining adequate symptomatic relief

f) has degenerative changes at 1 or 2 adjacent levels between L1-S1 confirmed by X-Ray, CT or MRI scan with one or more of the following:

- lumbar spinal stenosis with Neurogenic claudication
- decrease in disc height > 50%
- annular thickening
- degenerative Spondylolisthesis ≤ Meyerding Grade 1
- thickening of ligamentum flavum

g) is physically and mentally willing and able to comply with the postoperative scheduled clinical and radiographic evaluations.

3.4.4. **Exclusion Criteria**

A patient will not be admitted into the study if he/she meets any of the following exclusion criteria:

a) fixed motor deficit

b) is skeletally immature

c) has undergone previous lumbar spinal surgery

d) has obvious signs of psychological[i] or worker compensation or litigation claims[ii] elements to their condition

e) is unwilling or unable to give consent or adhere to the follow-up programme

f) has active infection or metastatic disease

g) has non-degenerative spondylolisthesis

h) has degenerative spondylolisthesis > Meyerding Grade 1

i) has a known allergy to implant materials

j) has severe osteoporosis or rheumatoid arthritis

k) cauda equina syndrome

l) acute disc extrusion or sequestered fragments

3.5. Hypothesis

The null hypothesis is stated as:

"There is no difference in cost effectiveness of the X-stop device compared to that of conventional decompressive surgery."

The null hypothesis will be rejected if the mean cost of treatment in the X-stop group is significantly different to the decompressive surgery group. Two-way analysis of variance will be performed to determine any statistically significant difference between the mean costs of treatment in the X-stop and decompression groups (p=0.05).

3.6. Sample size calculation

The sample size calculation is done by statistician and is based on a comparison of short-term costs between the randomised groups using a standard 2 sample t-test approach. Katz et al 1997 estimate mean hospital cost for lumbar laminectomy at £6639, with a standard deviation £1879.(149)

The consideration was made to detect at least a 20% difference in costs between the laminectomy and X-stop groups. In calculating sample size, an assumption of normality is considered acceptable since similar costs were noted to be symmetrically distributed by Katz et al. To detect at least a 20% difference with a 5% significance level and 90% power requires 43 patients per group. This number also allows 80% power to detect at least a 20% difference in the SF36 physical functioning scale at a 5% significance level (assuming mean after laminectomy of

72, standard deviation 22.8). The study by Katz et al suggests a dropout rate of up to 27% over a 2-year follow-up. To allow for this in the analysis of long-term outcomes we have inflated the sample size accordingly, requiring a minimum of 55 patients per group.

For clinical efficacy, 40 patients per group would allow us to detect at least a 20% difference in the SF36 physical functioning scale at a 5% significance level, 80% power. This calculation has used estimates from a previous study which reported mean (sd) for SF36 physical functioning score after laminectomy of 72 (22.8). (150) The method is based on a 2 sample t-test which requires assumptions of Normality and equal variance. The study by Katz et al, 1997 suggests a dropout rate of up to 27% over a 2-year follow-up.

3.7. **Operative techniques**

3.7.1. Lumbar laminectomy

Under general anaesthetic patients were positioned in the prone position in a theatre table which was adjusted to flex their spine. After the operative level(s) were confirmed through fluoroscopy, a mid-sagittal incision was made over the spinous processes of the stenotic level(s) and the musculature was elevated to the level of laminae and facets. Then laminae were removed over the stenotic segment. Skin closure was made.

3.7.2. X-stop device insertion

Under general anaesthetic patients were positioned in the prone position in a theatre table which was adjusted to flex their spine. After the operative level(s) were confirmed through fluoroscopy, a mid-sagittal incision was made over the spinous processes of the stenotic level(s) and the musculature was elevated to the level of laminae and facets. Occasionally, hypertrophied facets that blocked entry to the anterior interspinous space were partially trimmed to enable anterior placement of the implant. A curved dilator was inserted in the anterior margin of the interspinous space to pierce the interspinous ligament. A sizing distractor was then inserted to determine the appropriate implant size. The X-STOP was then secured to the

insertion instrument and inserted into the interspinous space.An attempt was made to place the implant as close to the posterior aspect of the lamina as possible. An adjustable wing was fastened to the implant and positioned as close to the midline as possible.The incision was closed

3.8. Outcome measures

3.8.1. Measuring costs

Costs were measured in UK Sterling (2010) as a sum of costs incurred for theatre time, inhospital stay, implant costs, physiotherapy sessions, outpatient clinic appointments attended and imaging.

3.8.2. *Measuring quality of life*

Quality of life is measured by general outcome measures such as EQ5D and SF36. The EQ-5D derives its name from the European Group (EuroQoL) that originally created the EQ-5D. (151) It is made up of 5 dimensions: Mobility, Self-Care, Usual Activities, Pain/Discomfort, Anxiety/Depression. Each dimension consists of 3 levels as follows:

Level 1: indicating no problems

Level 2: indicating some problems

Level 3: indicating extreme problems.

A unique health state is then defined by combining 1 level from each of 5 dimensions. Each unique health state is then converted to a particular unique score between -0.594 (worst then death) and 1(perfect health). There is also EQ5D VAS score where patients need to score a value out of 100 in a range 0 (worst imaginable health state) and 100 (best imaginable health state). (151)

SF36 is a widely used quality of life questionnaire, developed in USA, which stands for Short Form and it is made up of 36 items divided between 8 domains with each domain attempting to capture a specific aspect of quality of life. The domains are: Bodily pain (BP), Physical function (PF), General health (GH), Role emotional

(RE), Vitality (VT), Social functioning (SF), Mental health(MH), Role physical (RP). The higher the percentage the better the quality of life for each domain.(152)

3.8.3. *Measuring utility values*

QALYs were calculated from two sources and analysed separately. The sources for QALY calculations are made from EQ5D score and SF36. The SF-36 scores were transformed to Health Utility Index (HUI2) on the basis of equations from Nicholet al. (153) Then, both EQ5D and HUI2 were transformed by linear transformation on a rating scale ranging from 0 ("death") to 1("full health").

Subsequently QALYs were calculated as a sum of products of QALYs gained with length of time (at 6 weeks, 6 months and 12 months) for each patient since the operation date for both treatment groups separately.

3.8.4. Measuring clinical effectiveness

Cost-effectiveness analysis of both interventions was performed by first measuring outcomes in terms of quality-adjusted life years (QALYs) and in terms of the incremental cost.

As explained earlier the ICER is calculated as the difference in costs lumbar laminectomy and X-stop groups incurred divided by the difference in QALYs accrued between the two treatments being compared. The term dominant is used to reflect instances in which one intervention is both less expensive and more effective (i.e., offers better quality of life) than the alternative intervention.

All results are expressed in UK sterling.

We represented uncertainty (secondary to sampling variation in the cost-effectiveness ratios) by using the stochastic (bootstrapping) and probabilistic techniques (Monte Carlo simulation), to generate the sampling distribution of the cost and efficacy (QALYs). This has enabled us to quantify the uncertainty surrounding the estimates of costs and effects, presented graphically on the cost-effectiveness plane. We generated 1000 bootstrap replications of the cost-effectiveness ratios.(147)

3.8.4.1. Sensitivity Analyses

Sensitivity analyses were performed to determine the consequences of making alternative assumptions, for instance, about the definition of treatment success regarding the number of affected levels.

One-way sensitivity analysis was used to test the robustness of the results and to determine if the number of levels operated have a substantial effect on the results. The results generated by the cost-effectiveness model are considered robust because the cost effectiveness ratios fall within a narrow range when key model assumptions and parameters are varied.

3.8.4.2. Uncertainty in cost-effectiveness

For the decision -maker to make a decision regarding the reimbursement of a new technology, the emphasis will lie in the probability that the new technology is cost-effective compared to the existing alternative. This can be deduced from the incremental cost-effectiveness plane when compared to maximum acceptable ceiling ratio represented by the cost-effectiveness acceptability curve (CEAC). The maximum acceptable ceiling ratio represents the values that decision makers are willing to pay for the use of particular treatments. In practice, the maximum acceptability ceiling ratios represent the proportion of the incremental cost-effect pairs that fall to the south east of a line with slope through the origin. The CEAC indicates the probability that an intervention is cost-effective compared with the alternative, given the observed data, for a range of maximum acceptability ratio values.

*3.8.5. **Measuring clinical outcomes***

Clinical outcomes in this study were measured using the following disease-specific questionnaires:

3.8.5.1. *Zurich Claudication Questionnaire (ZCQ):-* This is an instrument widely used in lumbar stenosis patients with excellent reliability, validity and responsiveness. (154) (155)

It consists of three components:

1. Symptom component (rated on a scale of 1 – 5)
2. Physical component (rated on scale 1- 4).
3. Satisfaction component (rated on scale 1-4)

The maximum score for each component is represented as percentage of total score of each component.

3.8.5.2. *Oswestry Disability Index (ODI):-* The Oswestry Disability Index (ODI)(156) have emerged as one of the most commonly recommended condition specific outcome measures for spinal disorders.(157) (158)
It is made up of 10 sections each comprising of 5 questions. The score is calculated as the percentage of the total. The higher the score the worse is the outcome.(159)

3.8.5.3. *Quebeck Back Pain Disability Scale (QBPDS):-* This is an additional disease –specific test used to encompass more outcome features as the ODI, for example, does not include body movements such as bending or pushing. QBPDS is thought to be highly sensitive and reliable in lower back pain conditions. (160)

3.9. Time line

The following assessments will take place preoperatively and at following follow-up periods - 6 weeks, 6 and 12 months:

- EQ5D (also at discharge),
- SF36
- QBPDS
- Oswestry Disability Index (ODI)
- Zurich Claudication Questionnaire (ZCQ) (Symptom and Satisfaction component also at discharge)

3.10. Radiological data

The changes between preoperative and postoperative changes were analysed for the following radiological features:
-spinal canal area, foraminal area, facet size, anterior and posterior disc heights, inetrvertebral angles, Cobb angle.
The spinal canal area was calculated as an average of the anterior-posterior diameter and transverse diameter of the spinal canal divided by two which gives the radius.The formula for the area of the circle was utilised as follows:

Area of circle (mm^2)= π x $Radius^2$ = π x $(average\ diameter/2)^2$
where π = 3.1415926535 (pi value) and
average diameter = (anteriorposterior diameter +transverse diameter)/2

The patients were positioned in such a way in the MRI scanner to preserve the angle of cuts and patients were entered in the scanner head first. There were no claustrophobic patients in this study which would have required different means of positioning (leg first or open MRI scanners) The imaging cuts were consistently done parallel to the discs so that a more representative homogenous spinal canal area is obtained.

Also, the radiological parameters for the upper and lower adjacent vertebral levels to the operated level(s) were analysed such as: -Spinal canal, foraminal area, ligamentum flavum thickness, disc heights

3.11. Complication and Reoperation rates

We report on complications encountered and on the reoperation rate for patients in both treatment groups.

3.12. Statistical Analysis

Continuous data with more than two groups were analysed by:

- two-way ANOVA (with two factors such as Procedure (Lumbar laminectomy versus X-stop) and Period (preoperative, discharge, 6-weeks, 6-monhts and 12-months data)),
- one-way ANOVA
- Student's t-test 2-sample testing

-Mann Whitney non-parametric testing –for data which were either skewed and untransformable, or too few.

Discrete data were analysed by chi-squared.

Simple regression was used to assess convergent validity of general outcome instruments such as EQ5D and SF36 domains.

Multivariate linear regression analysis, logistic regression and log-linear modelling

GenStat 10th edition was the statistical software package used to analyse the results.

3.13. Intention to treat analysis

The participants are counted in the treatment group to which they were allocated by randomization, even if they later switch treatments.

3.14. Ethical Considerations

Ethics Committee Approval

The Charing Cross Research Ethics Committee (Type 3) has granted favourable opinion to proceed with the study (Ref No: 08/H0711/12) will be required prior to starting the study because of the randomised design.

Declaration of Helsinki

This study is conducted in accordance with the relevant articles of the Declaration of Helsinki as adopted by the 18th World Medical Assembly in 1964 and as revised in Tokyo (1975), Venice (1983), Hong Kong (1989), South Africa (1996) and Edinburgh (2000).

4. RESULTS

4.1. ***Recruitment***

In this study, 26 patients were eligible of which 6 were excluded (Table 4.1) and the other 20 were randomised into two groups. From the excluded patients, 2 patients did not want any operation and opted for conservative treatment, 2 patients were untraceable as changed the address, 1 patient developed a persisting confusion state following the operation hence was not able to complete the questionnaires and did not undergo post-operative MRI Lumbar spine, and1 patient was found to have lung malignancy prior to procedure therefore excluded from the study as per our exclusion criteria. From 20 patients randomised in the study 10 patients were randomised to Lumbar laminectomy and the other 10 to X-stop groups (Fig 4.1).

Table 4.1: Reasons for exclusion

Reason	**Number of patients**
Unwilling to be operated	2
Untraceable-changed address	2
Confusion following the X-stop insertion	1
Incidental lung malignancy found preoperatively	1
Total excluded	6

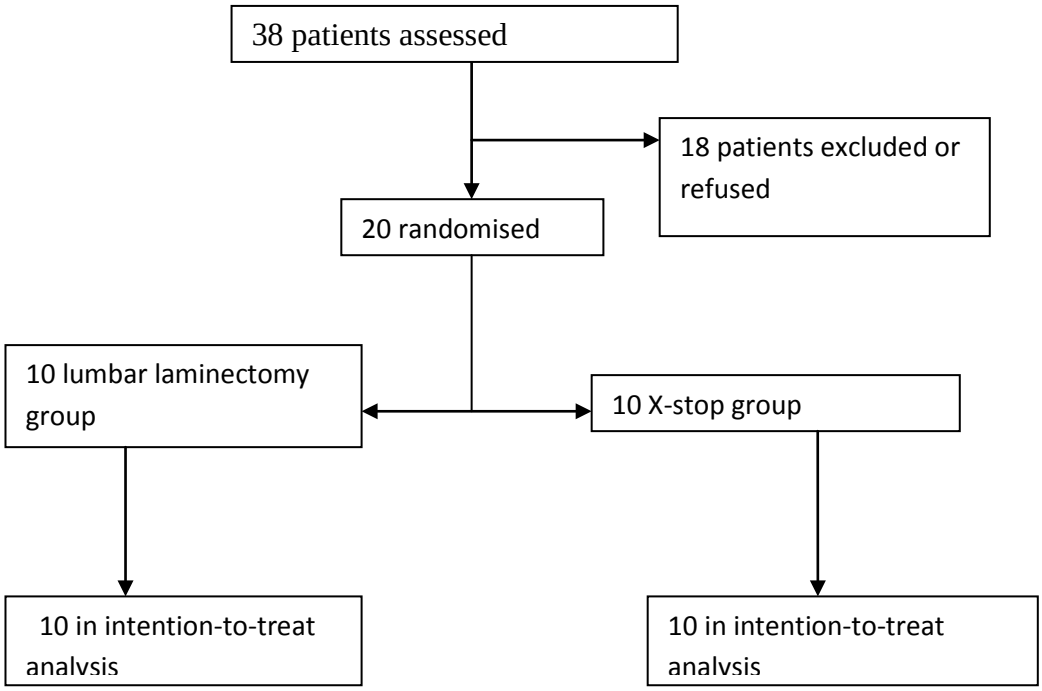


Figure 4.1: Flow chart of recruitment process

4.2. Demographics

Baseline demographic data of both treatment groups were comparable and statistically non-significant (Tables 4.2 & 4.3). Mean age was 66 in Lumbar laminectomy and 69.8 in X-stop group. Mean claudication distance in Lumbar laminectomy group was 104 meters and in X-stop group 218 meters. Mean duration of symptoms was 100 months in Lumbar laminectomy group and 50.6 months in X-stop group. Mean VAS score was 7.4 in Lumbar laminectomy and 7.6 in X-stop group (p=0.830). Male to Female ratio was about 1 in 2 in X-stop group and 1 in 1.5 in Lumbar laminectomy group.

We found that there were no differences in theatre time (p=0.454) (Figure 4.2A) as well as in-hospital stay (p=0.895) (Figure 4.2B) between the two treatment groups (Table 4.4).

Table 4.2: Baseline demographic data for continuous data: Age, Gender, Claudication distance and Duration of symptoms preoperatively. N=10 in each group; Students t-test used.

		Total			
	Procedure	Mean	SE	StDev	p-value
Age (years)	LL	66.00	1.99	6.31	0.322
	XS	69.80	3.13	9.89	
BMI(kg/m2)	LL	31.57	1.63	5.17	0.258
	XS	29.08	1.36	4.31	
Claudication Distance (metres)	LL	104.00	25.40	80.20	0.285
	XS	218.00	97.60	308.80	
Duration of Symptoms (months)	LL	100.80	27.40	86.80	0.184
	XS	50.60	23.70	74.80	
Visual Analogue Scale	LL	7.40	1.71	0.54	0.830
	XS	7.20	2.35	0.74	

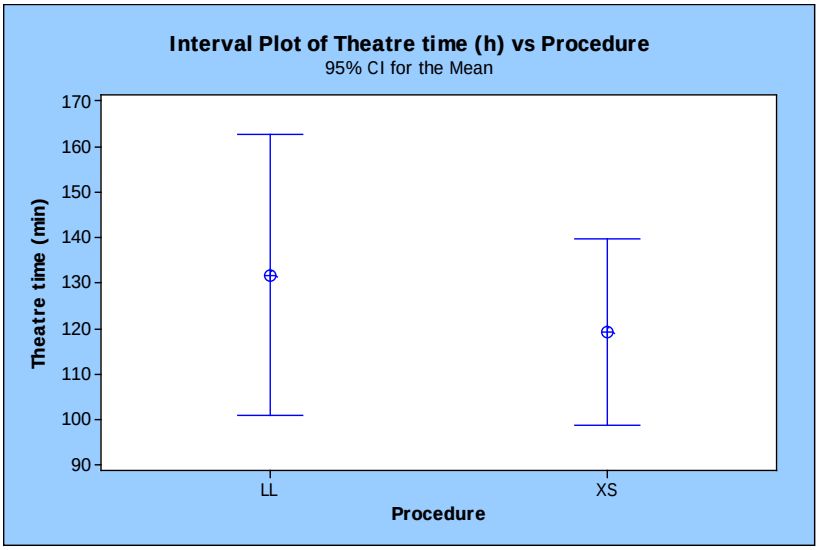
Table 4.3: Baseline demographic data for discrete data: Gender, Number of levels operated, Actual level(s) operated and Smoking status. N=10 in each group; Chi-squared test used.

		Counts (Percentage)		
Procedure		LL	XS	p-value
Gender				
Female	7(54)	6(46)	13(65)	0.639
Male	3(43)	4(57)	7(35)	
Number of levels operated				
1		6(43)	8(57)	0.329
2		4(67)	2(33)	
Total		10(50)	10(50)	
Actual level(s) operated				
L2/3		1(100)	0(0)	0.475
L3/4		3(60)	2(40)	
L4/5		3(33)	6(67)	
L2/3, L3/4		1(100)	0(0)	
L2/3, L4/5		0(0)	1(100)	
L34, L4/5		2(67)	1(33)	
Count		10(50)	10(50)	
Smoking status				
Smoker		4(40)	3(30)	0.639
Non-smoker		6(60)	7(70)	

In Lumbar laminectomy majority of patients (33%) were operated at L3/4 and L4/5 while majority of patient (67%) in X-stop group were operated at L4/5 (Table 3). One-level operation was performed in 43% of patients in lumbar laminectomy group, and 57% in X-stop group. Two-level operations were done in 67% of patients in Lumbar laminectomy group and 33% in X-stop group (Table 4.3).

Table 4.4: Theatre time and inhospital stay.

	Procedure	Mean	SE	StDev	p-value
Theatre time (min)	LL	131.70	13.70	43.20	0.454
	XS	119.10	9.06	28.66	
Inhospital stay (days)	LL	5.70	1.28	4.06	0.895
	XS	6.00	1.84	5.81	



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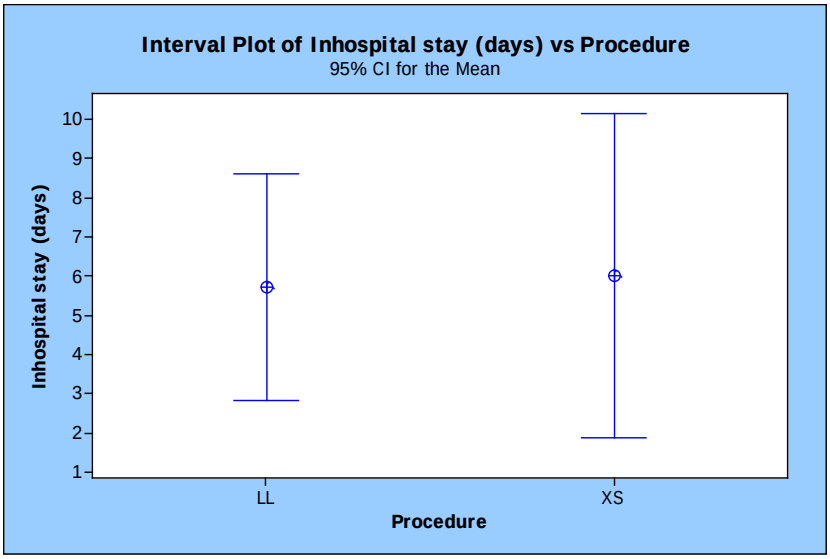


B)

Figure 4.2: A) Theatre time and B) Inhospital stay for Lumbar laminectomy and the X-stop groups.

4.3. Quality of life

As previously mentioned, quality of life was analysed using the EQ5D and SF36 outcome measures.

4.3.1. EQ5D Levels

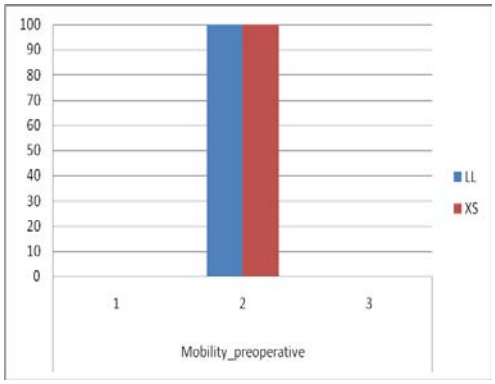
In our study log-linear modelling has shown that there is no statistically significant interaction between all five 5 dimensions (Mobility, Self care, Usual activities, Pain/Discomfort, Anxiety/Depression), treatment group and Period ($p>0.05$). Levels 1, 2, 3 represents worsening dimension ('1' best, '3' worst).

4.3.1.1. Mobility

There is baseline similar Mobility dimension scores between patient with all of them scoring 2 which is 'I have some problems in walking about' in both treatment groups with an improving trend at different Periods (Table 4.5 and Figure 4.3).

Table 4.5: Mobility dimension counts for each level of dimension for both treatment groups.

		Number of patients	
	OPERATION	LL	XS
MOBILITY	PERIOD		
1	12months	1	4
	6months	2	5
	6weeks	1	4
	Discharge	1	3
	Preoperative	0	0
2	12months	9	6
	6months	8	5
	6weeks	9	6
	Discharge	9	7
	Preoperative	10	10
3	12months	0	0
	6months	0	0
	6weeks	0	0
	Discharge	0	0
	Preoperative	0	0



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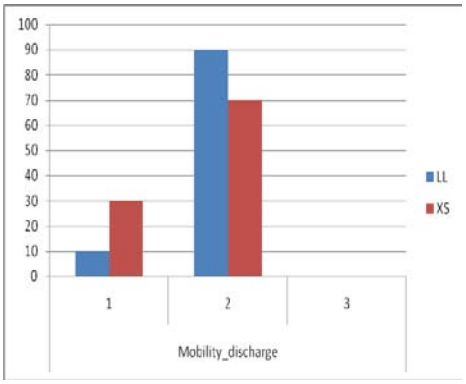

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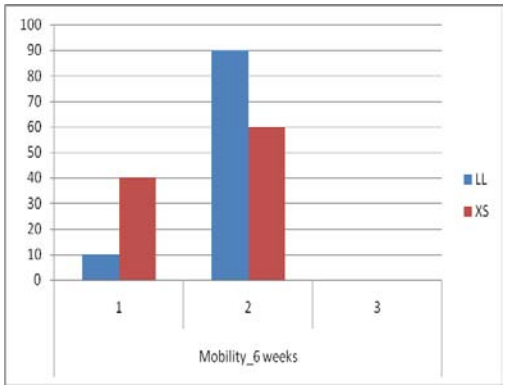

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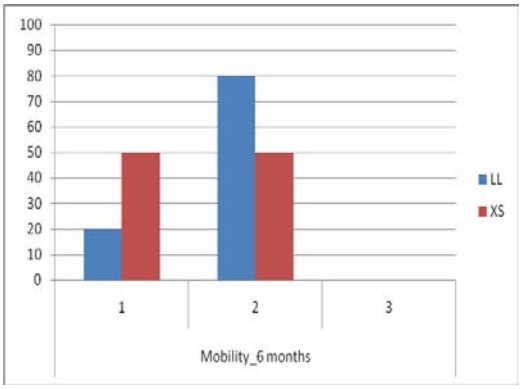

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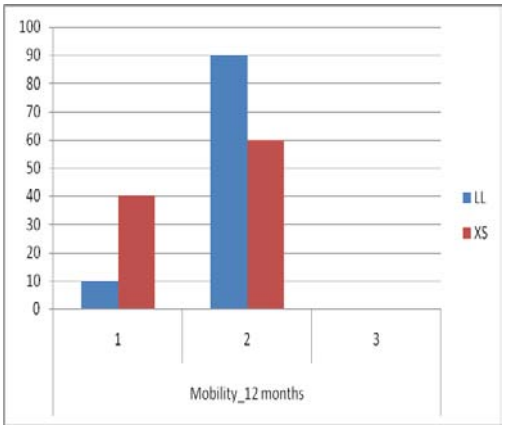


E)

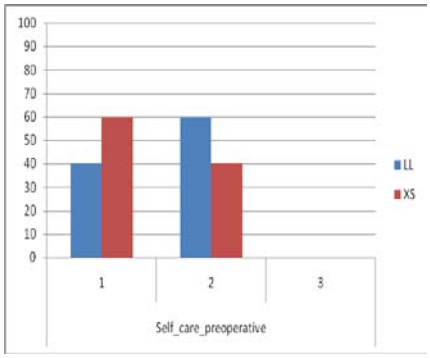
Figure 4.3: Mobility levels at different periods, A)Preoperative; B)Discharge; C) 6 weeks; D) 6 months; E) 12 months. Horizontal axis indicates levels of Mobility.

4.3.1.2. **Self-Care**

There was no trend in change in Self-care in Lumbar laminectomy group while there was a trend towards worsening in X-stop group. These changes were found to be non-significant (p>0.05) (Table 4.6 and Figure 4.4).

Table 4.6: Self Care dimension counts for each level of dimension for both treatment groups.

		Total Counts	
	OPERATION	LL	XS
SELF-CARE	PERIOD		
1	12months	4	5
	6months	4	4
	6weeks	6	5
	Discharge	3	4
	Preoperative	4	6
2	12months	6	4
	6months	6	5
	6weeks	4	5
	Discharge	4	5
	Preoperative	6	4
3	12months	0	1
	6months	0	1
	6weeks	0	0
	Discharge	3	1
	Preoperative	0	0



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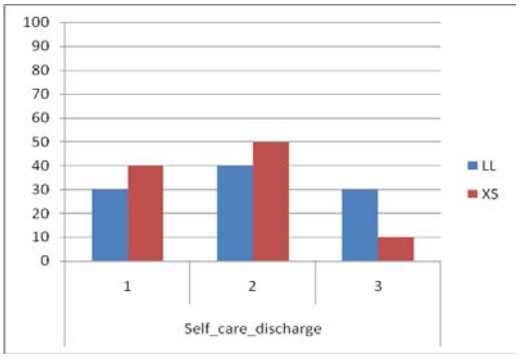

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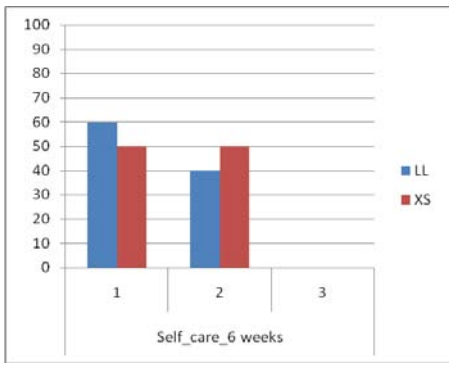

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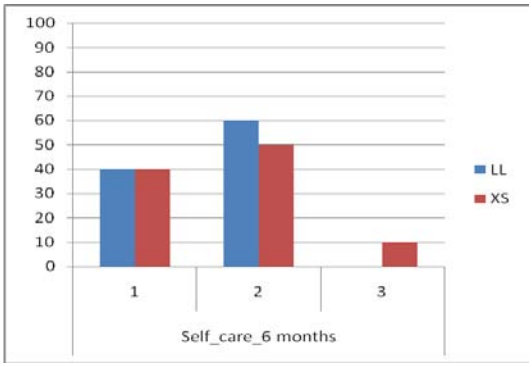

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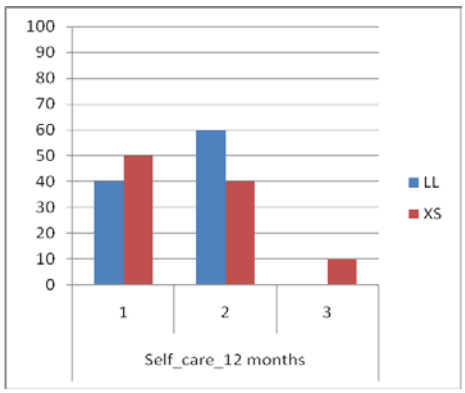


E)

Figure 4.4: Self-Care levels at different periods, A)Preoperative; B)Discharge; C) 6 weeks; D) 6 months; E) 12 months. Horizontal axis indicates levels of Self-Care.

4.3.1.3. **Usual Activities**

There seems to be some improving trend in Usual Activities in X-stop group with somewhat unchanged trend in Lumbar laminectomy group. These changes were found to be non-significant ($p>0.05$) (Table 4.7 and Figure 4.5).

Table 4.7: Usual Activities dimension counts for each level of dimension for both treatment groups.

		Total Counts	
	OPERATION	LL	XS
USUAL-ACTIVITIES	PERIOD		
1	12months	1	3
	6months	1	3
	6weeks	2	4
	Discharge	1	2
	Preoperative	3	3
2	12months	7	5
	6months	8	3
	6weeks	6	4
	Discharge	6	8
	Preoperative	6	7
3	12months	2	2
	6months	1	4
	6weeks	2	2
	Discharge	3	0
	Preoperative	1	0

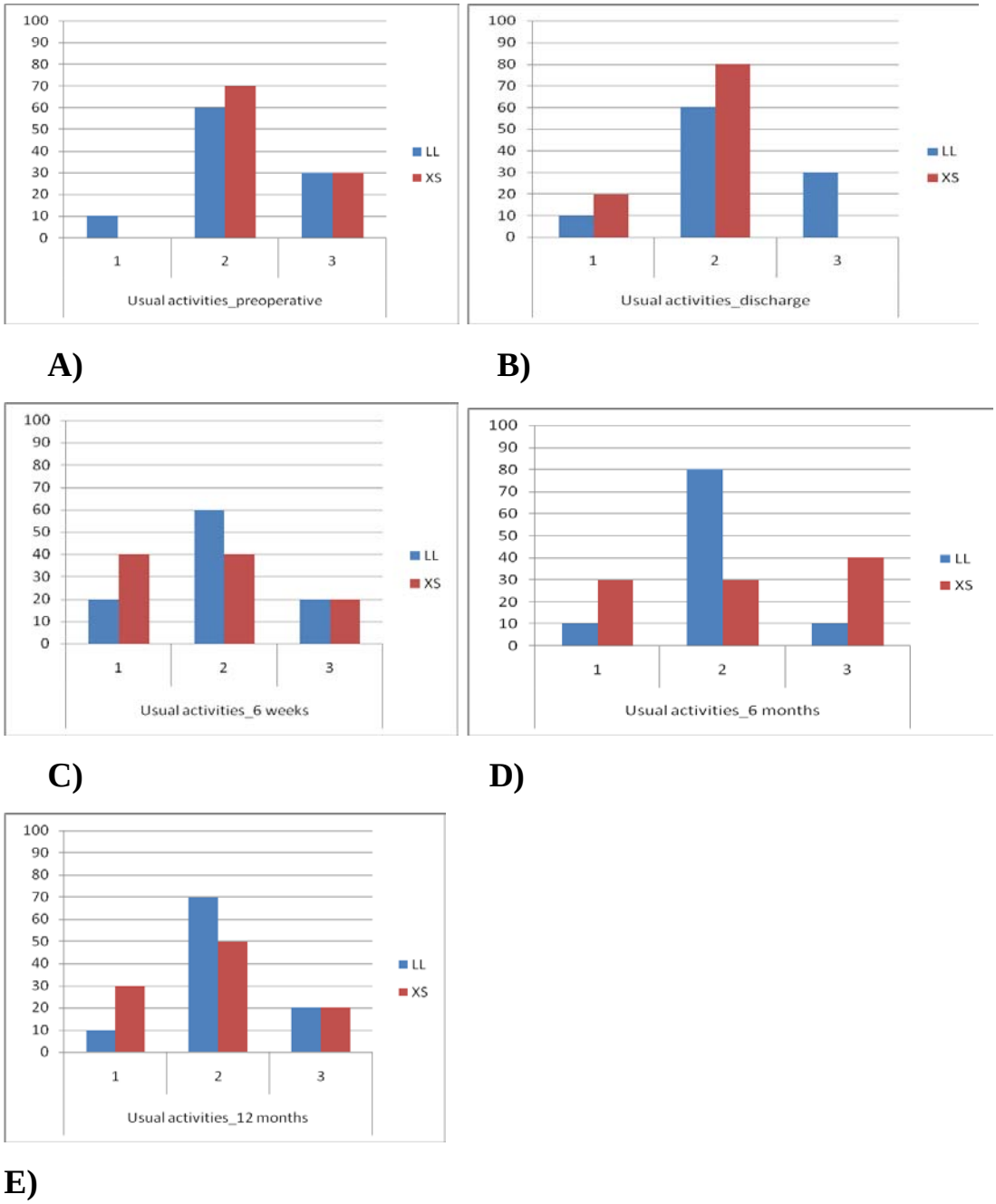


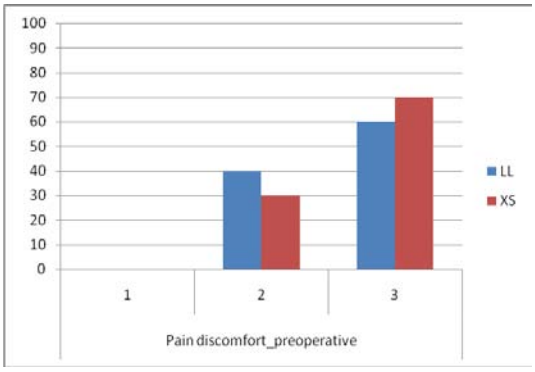
Figure 4.5: Usual Activities levels at different periods, A)Preoperative; B)Discharge; C) 6 weeks; D) 6 months; E) 12 months. Horizontal axis indicates levels of Usual Activities.

4.3.1.4. **Pain/Discomfort**

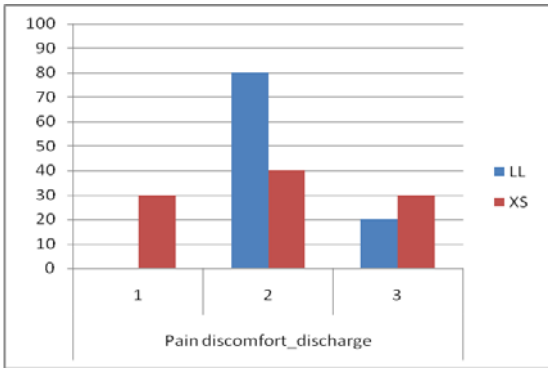
There seems to be an improving trend in Pain/discomfort levels across Lumbar laminectomy and X-stop group. These changes were found to be non-significant ($p>0.05$) (Table 4.8 and Figure 4.6).

Table 4.8: Pain/Discomfort dimension counts for each level of dimension for both treatment groups.

		Total Counts	
	OPERATION	LL	XS
PAIN_DISCOMFORT	PERIOD		
1	12months	1	1
	6months	1	1
	6weeks	1	1
	Discharge	0	3
	Preoperative	0	0
2	12months	7	6
	6months	6	6
	6weeks	8	6
	Discharge	8	4
	Preoperative	4	3
3	12months	2	3
	6months	3	3
	6weeks	1	3
	Discharge	2	3
	Preoperative	6	7



A)



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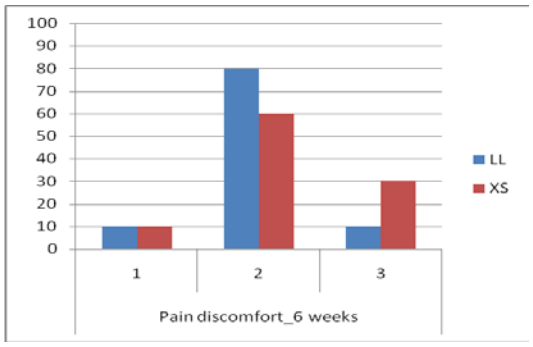

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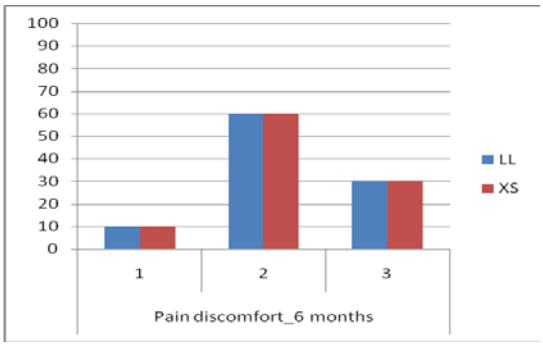

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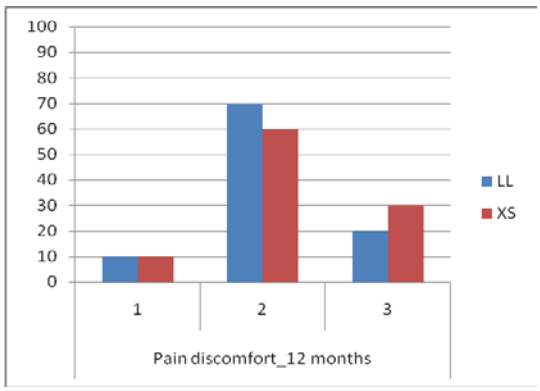


E)

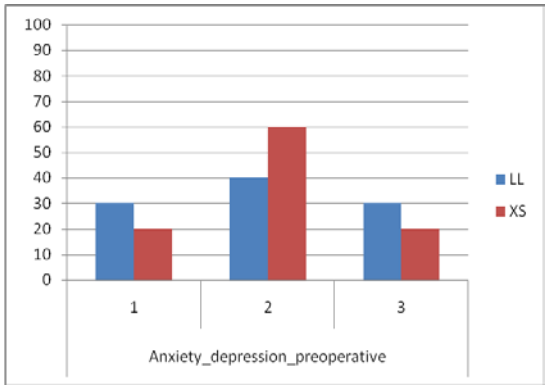
Figure 4.6: Pain/Discomfort levels at different periods, A)Preoperative; B)Discharge; C) 6 weeks; D) 6 months; E) 12 months. Horizontal axis indicates levels of Pain/Discomfort.

4.3.1.5. **Anxiety/Depression**

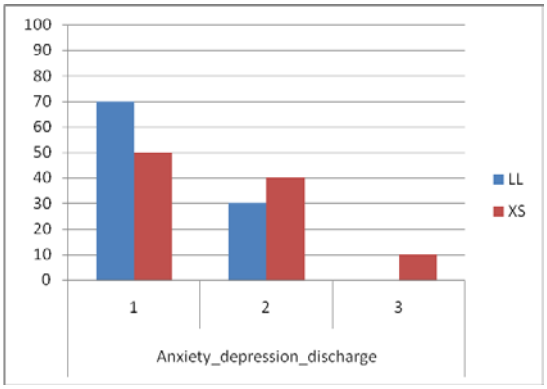
There is an improving trend in Anxiety/Depression which is statistically non-significant ($p>0.05$) (Table 4.9 and Figure 4.7).

Table 4.9: Anxiety/Depression dimension counts for each level of dimension for both treatment groups.

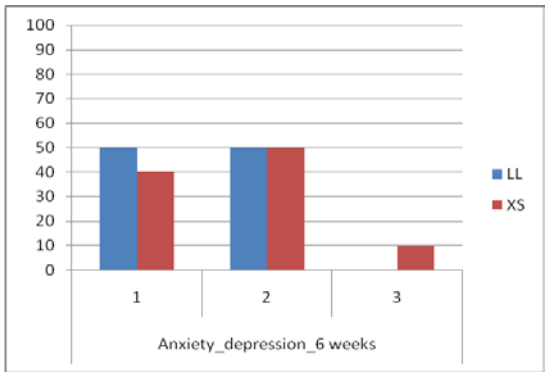
		Total Counts	
	OPERATION	LL	XS
ANXIETY DEPRESSION	PERIOD		
1	12months	6	5
	6months	5	4
	6weeks	5	4
	Discharge	7	5
	Preoperative	3	2
2	12months	3	4
	6months	4	4
	6weeks	5	5
	Discharge	3	4
	Preoperative	4	6
3	12months	1	1
	6months	1	2
	6weeks	0	1
	Discharge	0	1
	Preoperative	3	2



A)



B)



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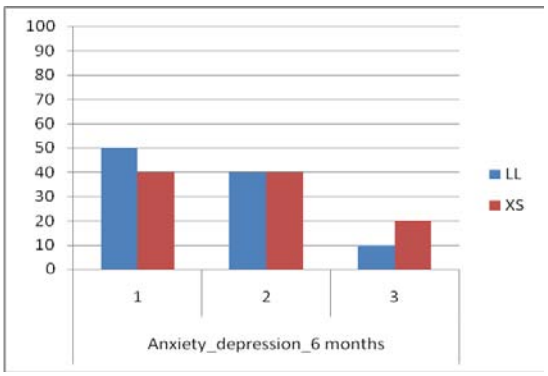

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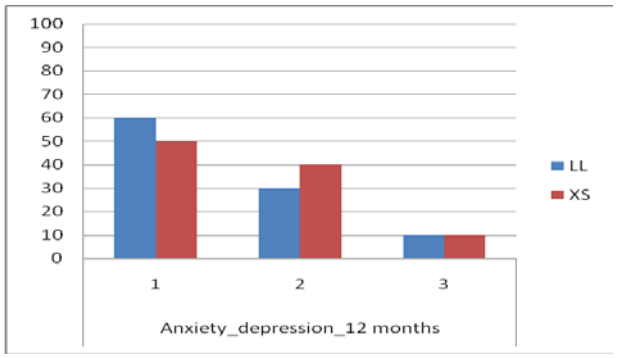


E)

Figure 4.7: Anxiety/Depression levels at different periods, A)Preoperative; B)Discharge; C) 6 weeks; D) 6 months; E) 12 months. Horizontal axis indicates levels of Anxiety/Depression.

4.3.2. **EQ5D scoring and EQ5D VAS**

The quality of life, as measured by EQ5D score, seems to be similar in both treatment groups per each period (Table 4.10A and Figure 4.8). However, the Two-way ANOVA assessing EQ5D score based on Procedure and Period, showed that there is a significant difference in EQ5D score at different periods (p=0.03) but there is no difference between the two treatment groups (p=0.965).

In addition, two-way ANOVA showed that there was no significant difference in EQ5D VAS at different periods (p=0.774) but with significant difference between the two treatment groups overall (p=0.029). This difference can be accounted by Lumbar laminectomy group starting with a better quality of life in EQ5D VAS scale in preoperative period (p=0.044) but in other periods there was no difference between the groups (p>0.05) ((Figure 4.9, Table 4.11)). This result is most likely due to natural variation in data considering that the trial was randomised with the aim of avoiding selection bias.

4.3.2.1. *Lumbar laminectomy group*

Further analysis using One-way ANOVA with contrast analysis of EQ5D score between preoperative and overall postoperative time period showed that there was a significant improvement of quality of life in Lumbar laminectomy (p=0.005, One way contrast ANOVA) but not in X-stop group. This improvement in quality of life in Lumbar laminectomy group is noted at discharge, 6 months and at 12 months (Table 4.10B).

4.3.2.2. X-stop group

There is an improving trend in quality of life in X-stop group (Table 4.10C, Figure 4.8, Figure 4.9), although this was not statistically significant across all time periods for EQ5D score (p=0.426, One-way ANOVA) and EQ5D VAS (p=0.649, One-way ANOVA). We did not detect statistical significance with further analysis, where preoperative and overall post-operative groups were compared for EQ5D score (p=0.089, One-way contrast ANOVA) and EQ5D VAS (p=0.153, One way contrast ANOVA). However, p-value of 0.089 could reflect the small sample size in the study to reach statistical significance.

There is an improving trend in quality of life, especially between preoperative and discharge periods (Figure 4.8) with small p-value of 0.072 (Table 4.10C) supporting the fact that our sample size may be too small to detect the differences statistically.

Table 4.10: EQ5D score at different periods. A) Between-group differences, B)Within-group in lumbar laminectomy (LL), C) Within- group in X-stop (XS). Note that in A) p-values indicate the strength of evidence between treatment groups in each period, while in B) and C) p-values indicate the strength of evidence between preoperative and other periods. RED text indicates significant results.

A)

Period	Procedure	Mean	SE	StDev	p-value
Preoperative	LL	0.116	0.065	0.205	0.679
	XS	0.170	0.111	0.350	
6-weeks	LL	0.557	0.094	0.298	0.392
	XS	0.417	0.128	0.403	
6-months	LL	0.390	0.126	0.399	0.802
	XS	0.342	0.141	0.445	
12-months	LL	0.470	0.101	0.320	0.849
	XS	0.437	0.138	0.437	

B)

	Period	Mean	SE	StDev	p-value
EQ5D_LL	12 months	0.470	0.101	0.320	0.009
	6 months	0.390	0.126	0.399	0.070
	6 weeks	0.557	0.094	0.298	0.001
	Discharge	0.370	0.100	0.317	0.048
	Preoperative	0.116	0.065	0.205	

C)

	Period	Mean	SE	StDev	p-value
EQ5D_XS	12 months	0.437	0.138	0.437	0.149
	6 months	0.342	0.141	0.445	0.400
	6 weeks	0.417	0.128	0.403	0.160
	Discharge	0.520	0.147	0.464	0.072
	Preoperative	0.170	0.111	0.350	

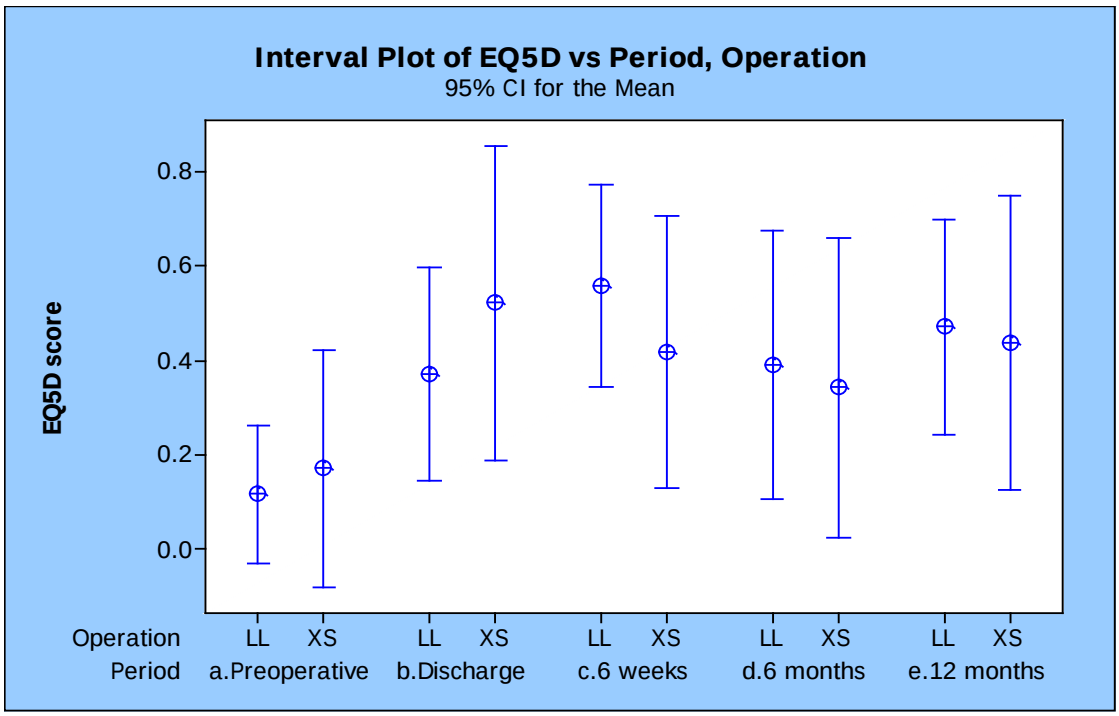


Figure 4.8: EQ5D score at different time points for both treatment groups. Data shown as 95% CI of the mean.

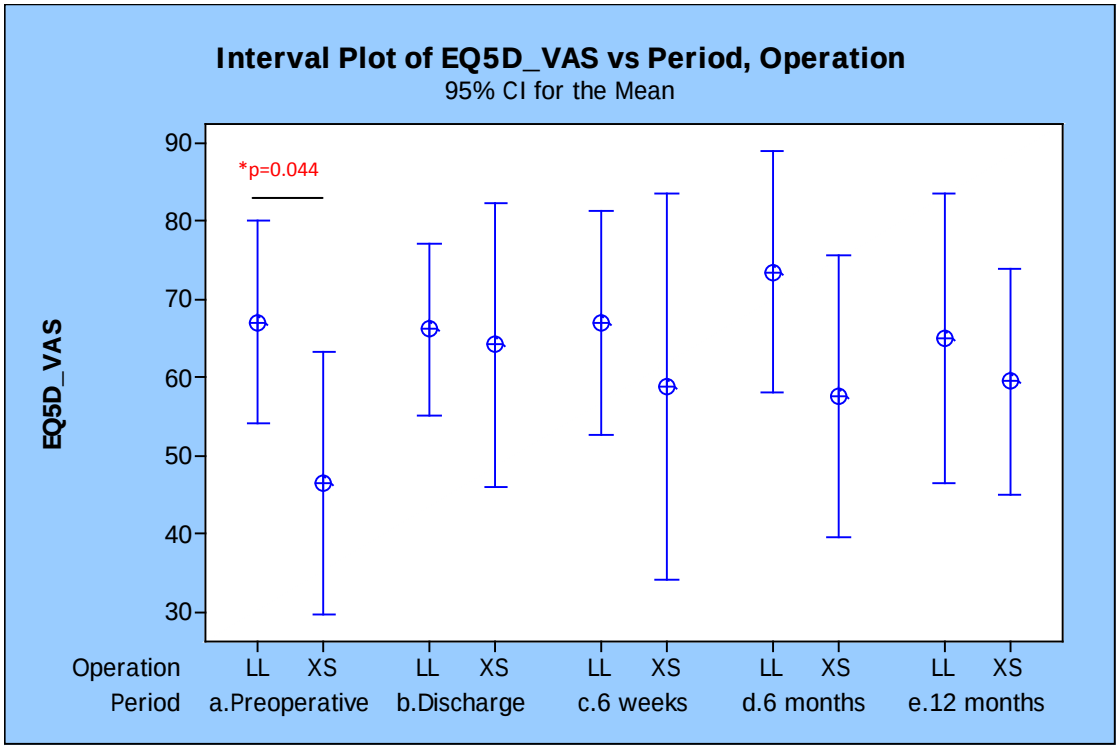


Figure 4.9: EQ5D VAS at different time points for both treatment groups. Data shown as 95% CI of the mean.

Table 4.11: EQ5D VAS at different periods. RED text indicates significant results.

EQ5D VAS

Period	Procedure	Mean	SE	StDev	p-value
Preoperative	LL	67.00	5.73	18.14	0.044
	XS	46.50	7.42	23.46	
Discharge	LL	66.20	4.86	15.38	0.835
	XS	64.20	8.04	25.42	
6-weeks	LL	67.00	6.33	20.03	0.522
	XS	58.70	10.9	34.50	
6-months	LL	73.50	6.79	21.48	0.146
	XS	57.50	8.00	25.30	
12-months	LL	65.00	8.20	25.93	0.604
	XS	59.50	6.39	20.20	

4.3.3. **SF36 Domains**

The quality of life as measured by SF36 instrument, which consists of 8 domains, showed that there were no significant differences between the two treatment groups for any of domains (Table 4.12). However, there are improving trends in Physical functioning, Bodily pain and Mental Health in Lumbar laminectomy group (Figure 4.10). There are also improving trends in Physical functioning, Role Physical, Bodily pain, Role emotional and Mental health in the X-stop group (Figure 4.10).

Statistically-significant improvements (Table 4.12) compared to the preoperative state were reached in the following:

- X-stop group: -Physical functioning ($p=0.034$, Mann Whitney test) at 6 weeks
  -Bodily pain ($p=0.028$, Mann Whitney test) at 12 months
- Lumbar laminectomy: - Bodily pain ($p=0.017$, Mann Whitney test) at 6 weeks

Table 4.12: Quality of life (using SF36 scores per domains) for Lumbar laminectomy versus X-stop treatment groups including p-values for each time points. Values are expressed as Median (Interquartile range)

	PF_{LL}	PF_{XS}	p	RP_{LL}	RP_{XS}	p	BP_{LL}	BP_{XS}	p	GH_{LL}	GH_{XS}	p	VT_{LL}	VT_{XS}	p	SF_{LL}	SF_{XS}	p	RE_{LL}	RE_{XS}	p	MH_{LL}	MH_{XS}	p
Preoperative	17.5(21.25)	25.0 (27.5)	0.820	25.0 (62.5)	12.5(62)	0.678	22(14)	22(9.5)	1.0	69.5(44)	52.5(43.2)	0.880	57.5(53)	47.5(40)	0.345	68.8(78)	50(44)	0.385	100(75)	16.7(75)	0.162	60(43)	60(31)	0.326
6 weeks	35(37.5)	50(50)	0.226	12.5(81.3)	0(100)	0.910	41(18)	31.5(45)	0.345	59.5(32)	50(48.2)	0.734	66(32.5)	32.5(30)	0.257	62.5(62)	50(37)	0.450	33(100)	16.7(100)	1.0	80(50)	62(29)	0.545
	0.212	***0.034**		0.597	0.880		***0.017**	0.678		0.880	0.970		0.705	1.0		0.910	0.910		0.241	0.940		0.940	0.623	
6 months	27.5(43.7)	40(48.7)	1.0	12.5(81)	37(100)	0.427	36(57)	46(54.2)	0.762	55(43.2)	41(45.7)	0.290	50(23.7)	52.5(42)	0.738	62.6(66)	69(78)	0.820	33.5(100)	33(75)	0.910	62(42)	62(38)	0.910
	0.150	0.174		0.734	0.406		0.406	0.257		0.970	0.364		0.597	0.406		0.450	0.650		0.385	0.545		0.940	0.273	
12 months	37.5(41.2)	35(63.7)	1.0	12.5(75)	37.5(100)	0.427	41(39)	51(28)	0.791	54.5(42)	42.5(42)	0.650	50(43.7)	52.5(37)	0.650	56.3(69)	56.(87)	1.0	66.7(100)	67(67)	0.596	78(41)	70(28)	0.940
	0.130	0.241		0.545	0.545		0.096	***0.028**		0.791	0.734		0.623	0.273		0.623	0.678		0.571	0.102		0.850	0.082	

Indices LL and XS stand for Lumbar laminectomy and X-stop groups respectively.

PF, Physical Functioning;

RP, Role Physical;

BP, Body Pains;

GH, General Health;

VT, Vitality;

SF, Social Functioning;

RE, Role Emotional;

MH, Mental Health

*, significant p-value <0.05. Student's t-test used.

RED text are the p-values of the domains between the two treatment groups corresponding each period (preoperative, 6 weeks, 6 months, 12 months)

BLUE text are the p-values of the preoperative values of domains and the other corresponding periods (6 weeks, 6 months, 12 months) for each treatment group.

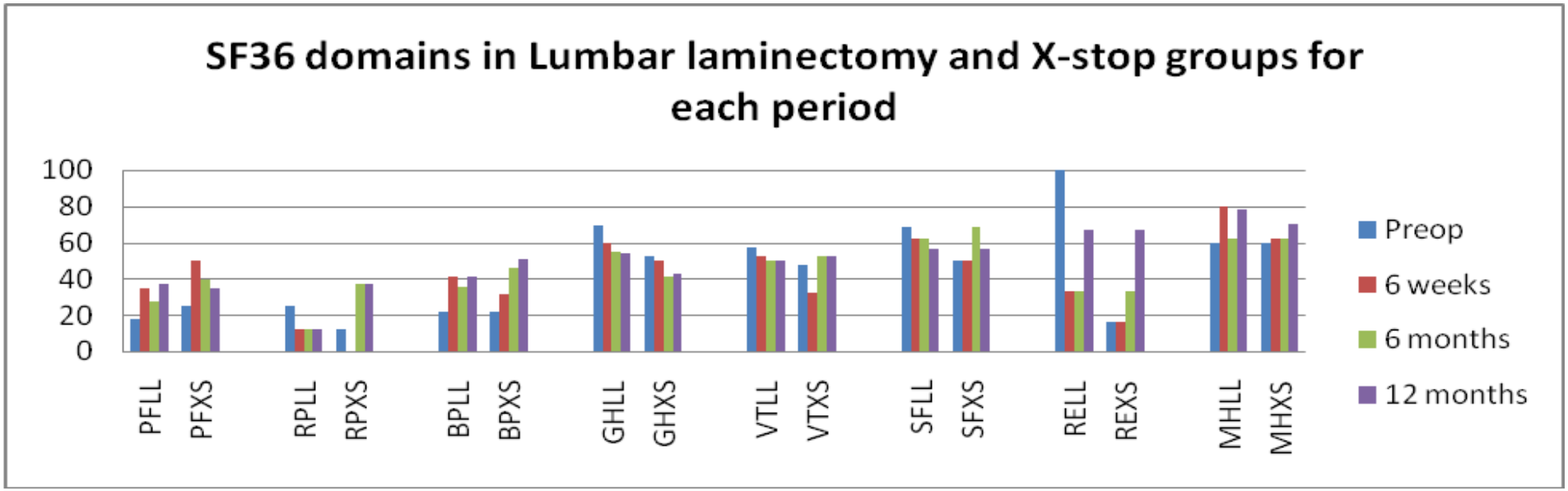


Figure 4.10: Quality of life domains for Lumbar laminectomy and X-stop for both treatment groups.

Note: Last two letters of each horizontal axis labels are LL, which stands for Lumbar laminectomy group, and XS stands for the X-stop group.

First two letters stand as described below:

PF, Physical Functioning;

RP, Role Physical;

BP, Body Pains;

GH, General Health;

VT, Vitality;

SF, Social Functioning;

RE, Role Emotional;

MH, Mental Health

Two way ANOVA with factorial analysis by Period and Procedure for each of the SF36 domains, showed that there were significantly greater Physical functioning between Periods (p=0.049) but not between Treatments (p=0.313) (Table 4.13). Further analysis by one-way ANOVA by Period for each Treatment for Physical functioning showed that there was overall no significant differences in Lumbar laminectomy group (p=0.065) and X-stop group (p=0.164). However, there was a significant overall improvement in Physical Functioning when preoperative and overall post-operative periods were compared within the X-stop group (p=0.043, One-way Contrast ANOVA).

In other domains no significant differences were found between Treatment groups for each Period or between Periods within each Treatment group.(Table 4.13)

Table 4.13: p-values for each domain of the SF36. Two-way factorial ANOVA performed on Period and Treatment groups. One-way ANOVA performed for each treatment groups.

	Two-way ANOVA		One-way ANOVA	
	Period	Treatment groups	Lumbar laminectomy	X-stop
BP	0.115	0.594	0.436	0.206
PF	0.049	0.313	0.294	0.164
RP	0.892	0.478	0.979	0.732
GH	0.805	0.453	0.985	0.761
VT	0.958	0.493	0.936	0.550
SF	0.989	0.498	0.883	0.975
MH	0.603	0.396	0.947	0.223
RE	0.531	0.446	0.621	0.368

4.3.3.1. **Bodily pain**

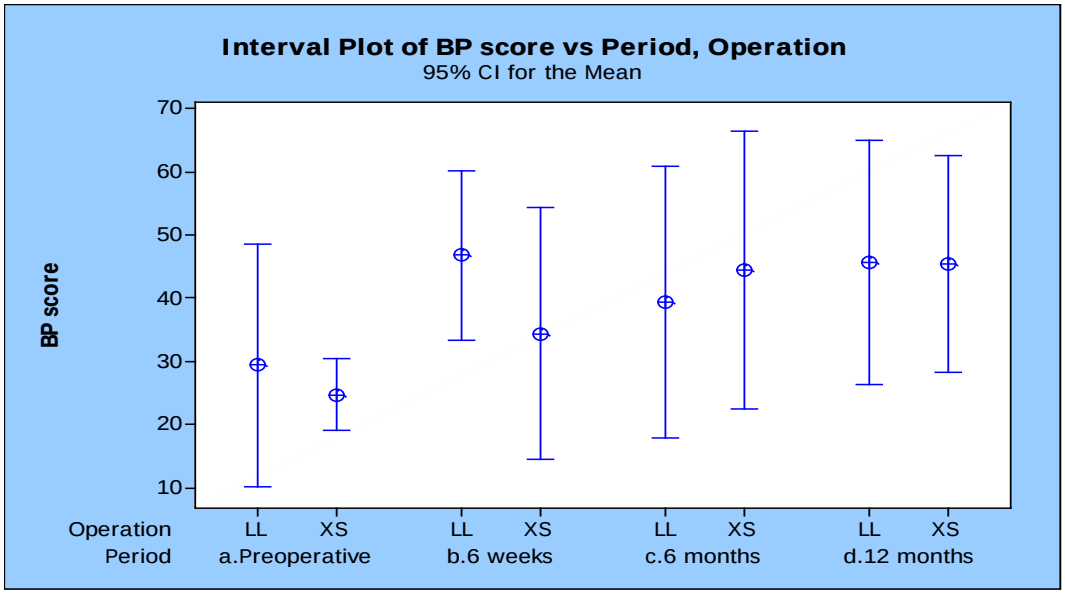


Figure 4.11: Bodily pains (percentage) across time periods for both treatment groups

Table 4.14: Bodily pains (percentage) descriptive data, SE=Standard error; StDev=Standard deviation

	Operation	Mean	SE	StDev
Preoperative				
	LL	29.40	8.54	27.00
	XS	24.70	2.52	7.96
6 weeks				
	LL	46.80	5.93	18.75
	XS	34.40	8.83	27.93
6 months				
	LL	39.30	9.54	30.16
	XS	44.50	9.74	30.81
12 months				
	LL	45.60	8.57	27.09
	XS	45.40	7.61	24.07

4.3.3.2. **Physical Functioning**

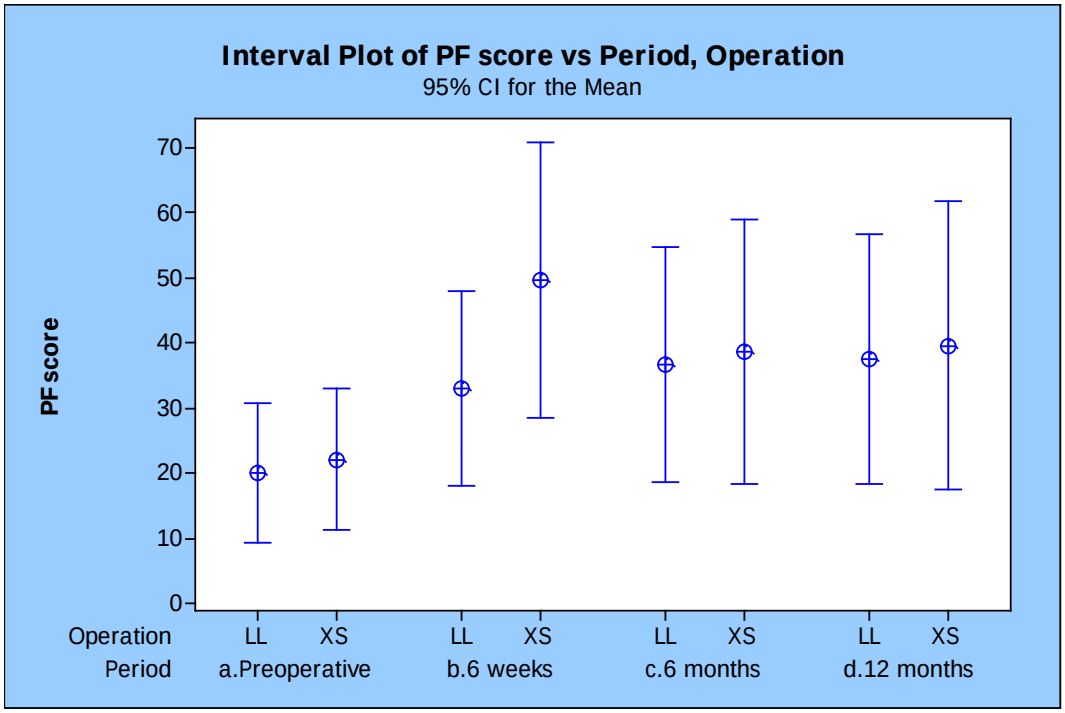


Figure 4.12: Physical functioning (percentage) across time periods for both treatment groups

Table 4.15: Physical functioning (percentage) descriptive data, SE=Standard error; StDev=Standard deviation

	Operation	Mean	SE	StDev
Preoperative				
	LL	20.00	4.77	15.09
	XS	22.00	4.78	15.13
6 weeks				
	LL	33.00	6.63	20.98
	XS	49.50	9.38	29.67
6 months				
	LL	36.50	7.99	25.28
	XS	38.50	8.98	28.39
12 months				
	LL	37.50	8.47	26.80
	XS	39.50	9.79	30.95

4.3.3.2. **Role physical**

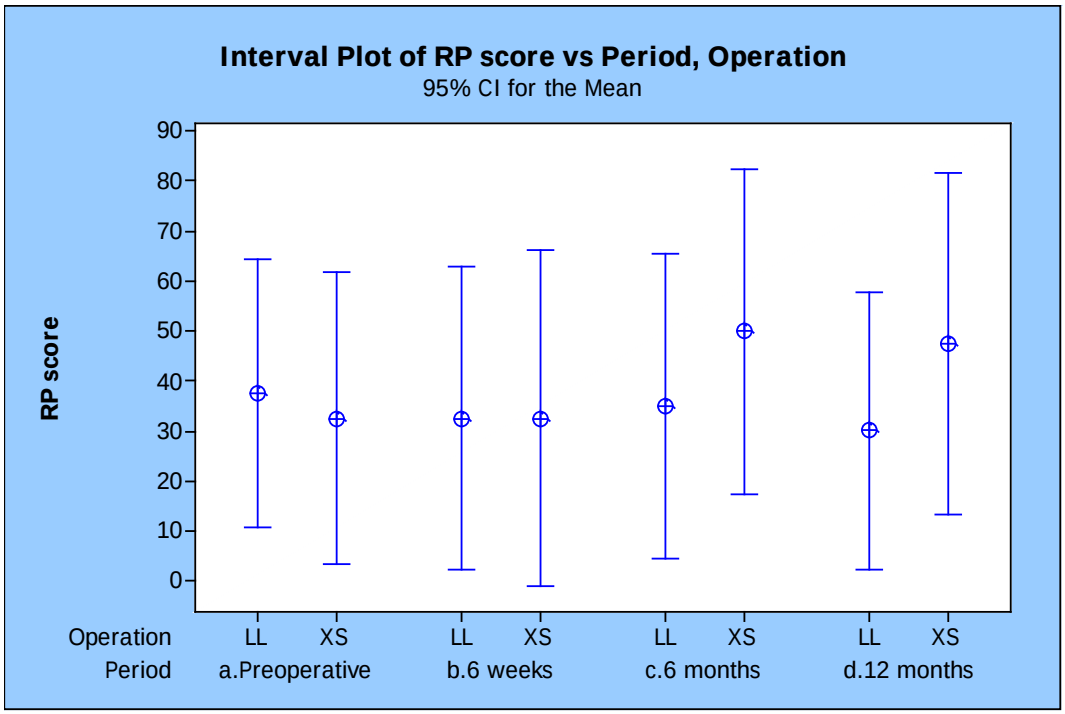


Figure 4.13: Role physical (percentage) across time periods for both treatment groups

Table 4.16: Role physical (percentage) descriptive data, SE=Standard error; StDev=Standard deviation

	Operation	Mean	SE	StDev
Preoperative				
	LL	37.5	11.9	37.7
	XS	32.5	12.9	40.9
6 weeks				
	LL	32.5	13.5	42.6
	XS	32.5	14.9	47.2
6 months				
	LL	35.0	13.5	42.8
	XS	50.0	14.4	45.6
12 months				
	LL	30.0	12.2	38.7
	XS	47.5	15.1	47.8

4.3.3.3. **General Health**

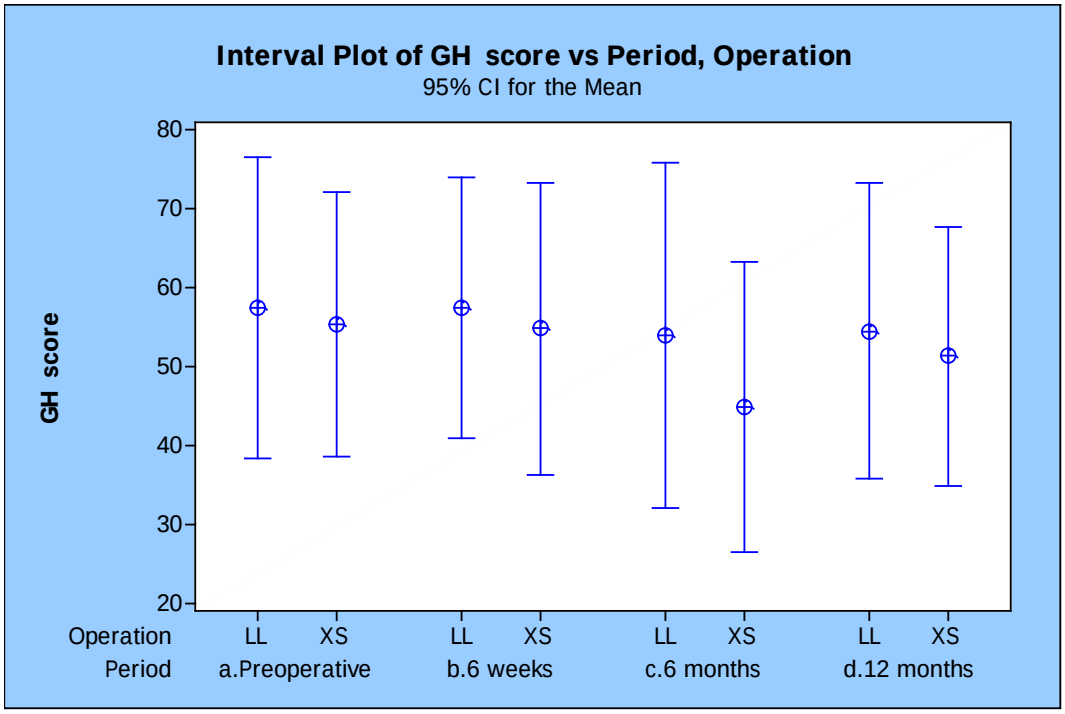


Figure 4.14: General health (percentage) across time periods for both treatment groups

Table 4.17: Role physical (percentage) descriptive data, SE=Standard error; StDev=Standard deviation

	Operation	Mean	SE	StDev
Preoperative				
	LL	57.50	8.44	26.69
	XS	55.30	7.42	23.45
6 weeks				
	LL	57.50	7.29	23.05
	XS	54.80	8.18	25.85
6 months				
	LL	54.00	9.67	30.59
	XS	44.80	8.13	25.72
12 months				
	LL	54.50	8.27	26.15
	XS	51.30	7.23	22.86

4.3.3.4. **Vitality**

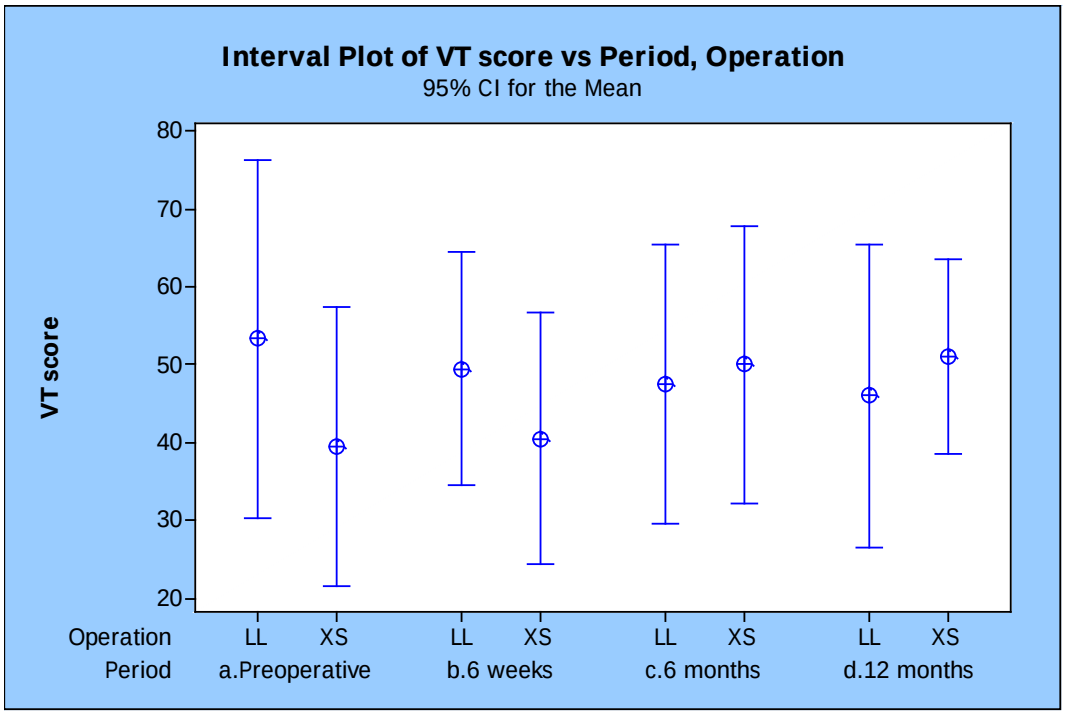


Figure 4.15: Vitality (percentage) across time periods for both treatment groups

Table 4.18: Vitality (percentage) descriptive data, SE=Standard error; StDev=Standard deviation

	Operation	Mean	SE	StDev
Preoperative				
	LL	53.30	10.2	32.20
	XS	39.50	7.97	25.22
6 weeks				
	LL	49.50	6.60	20.88
	XS	40.50	7.17	22.66
6 months				
	LL	47.50	7.97	25.19
	XS	50.00	7.85	24.83
12 months				
	LL	46.00	8.65	27.37
	XS	51.00	5.57	17.61

Social functioning

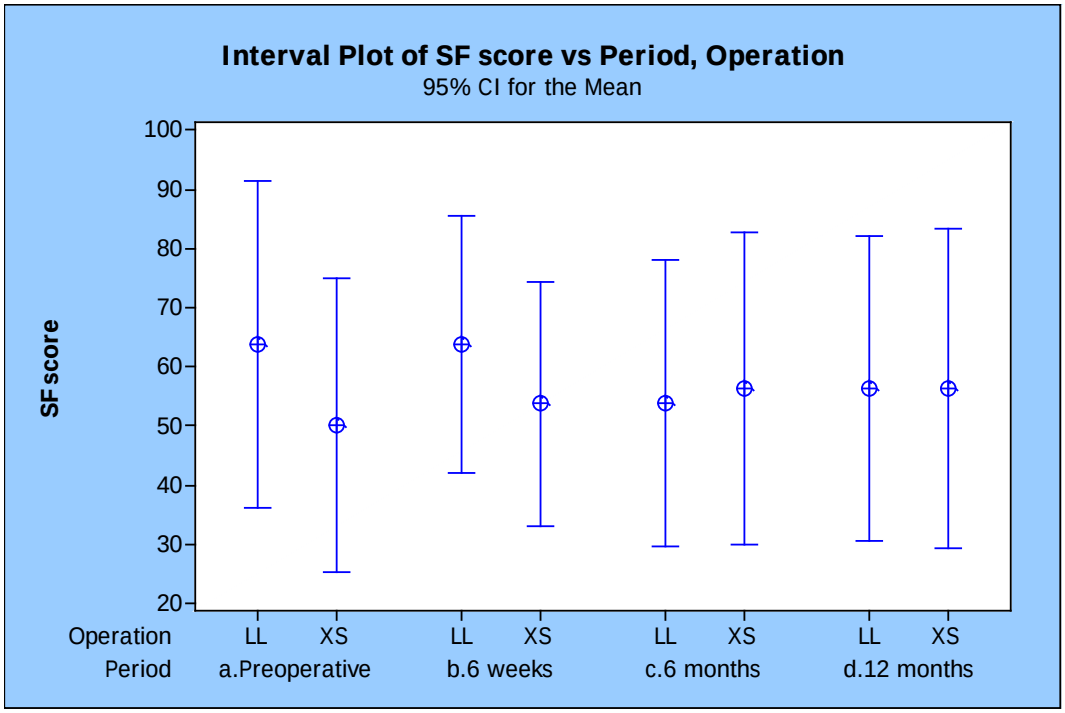


Figure 4.16: Social functioning (percentage) across time periods for both treatment groups

Table 4.19: Social functioning (percentage) descriptive data, SE=Standard error; StDev=Standard deviation

	Operation	Mean	SE	StDev
Preoperative				
	LL	63.80	12.30	38.80
	XS	50.00	11.00	34.90
6 weeks				
	LL	63.75	9.58	30.31
	XS	53.75	9.14	28.90
6 months				
	LL	53.80	10.70	33.90
	XS	56.30	11.70	36.90
12 months				
	LL	56.30	11.40	36.00
	XS	56.30	12.00	37.80

4.3.3.5. **Role Emotional**

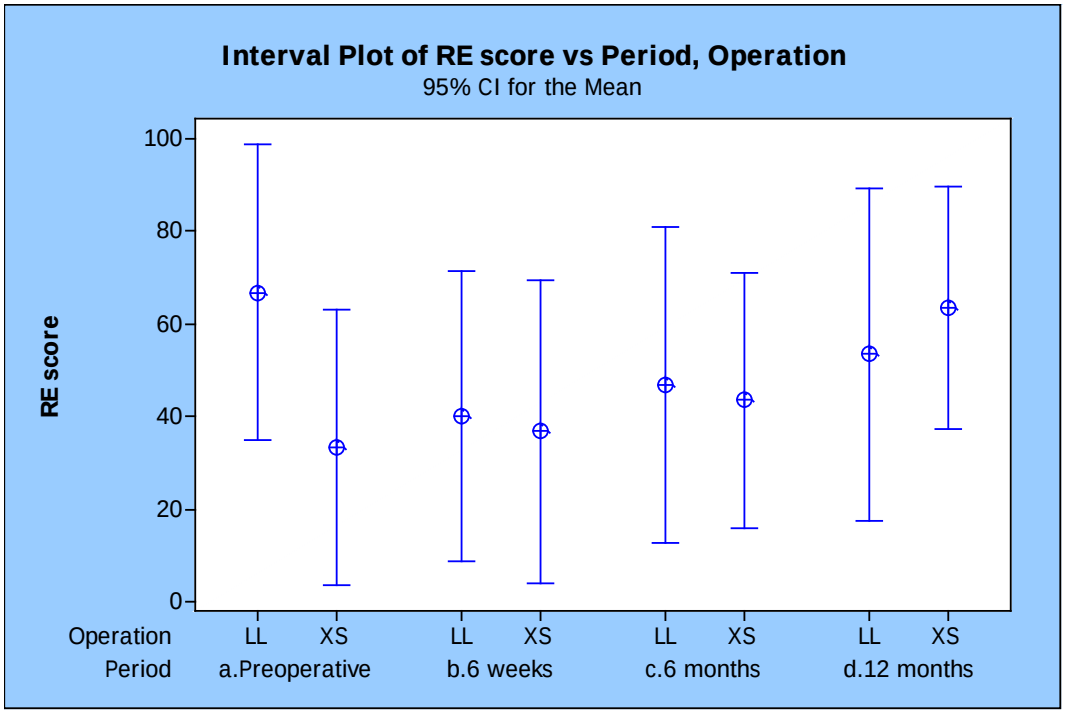


Figure 4.17: Role emotional (percentage) across time periods for both treatment groups

Table 4.20: Role emotional (percentage) descriptive data, SE=Standard error; StDev=Standard deviation

	Operation	Mean	SE	StDev
Preoperative				
	LL	66.7	14.1	44.4
	XS	33.3	13.1	41.6
6 weeks				
	LL	40.0	13.9	43.9
	XS	36.7	14.4	45.7
6 months				
	LL	46.7	15.1	47.7
	XS	43.3	12.2	38.7
12 months				
	LL	53.3	15.9	50.2
	XS	63.3	11.6	36.7

4.3.3.6. **Mental health**

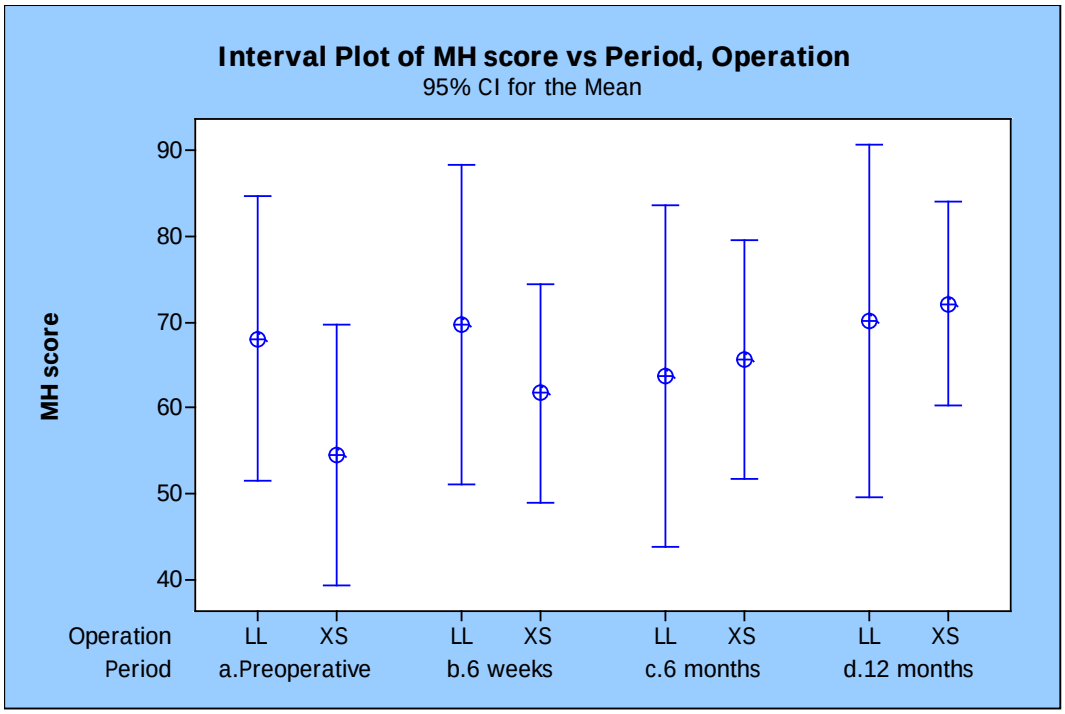


Figure 4.18: Mental health (percentage) across time periods for both treatment groups.

Table 4.21: Mental health (percentage) descriptive data, SE=Standard error; StDev=Standard deviation

	Operation	Mean	SE	StDev
Preoperative				
	LL	68.00	7.38	23.32
	XS	54.40	6.70	21.18
6 weeks				
	LL	69.60	8.25	26.07
	XS	61.60	5.63	17.81
6 months				
	LL	63.60	8.79	27.81
	XS	65.60	6.14	19.43
12 months				
	LL	70.00	9.09	28.74
	XS	72.00	5.27	16.65

4.4. COST-EFFECTIVENESS RESULTS

4.4.1. Quality Adjusted Life Years (QALYs)

The QALYs were calculated and analysed using both QoL instruments: EQ5D and SF36.

QALYs(using EQ5D)

There were no significant differences in mean QALYs *per* patient associated with either intervention (p=0.654) (Table 22, Figure 19). The mean QALYs gained per patient were 0.072 with 95% CI (-0.261, 0.405) in Lumbar laminectomy compared to X-stop group.

QALYs(using SF36)

There were no significant differences in mean QALYs *per* patient associated with either intervention (p=0.654) (Table 22, Figure 19). The mean QALYs gained per patient were 0.024 QALYs with 95% CI (-0.175, 0.224) in Lumbar laminectomy compared to the X-stop group.

Table 4.22: Summary analysis of QALYs (using EQ5D for both treatment groups.

	Procedure	Mean	SE	StDev	p-value
QALY_EQ5D	LL	0.638	0.059	0.186	0.654
	XS	0.593	0.079	0.250	
QALY_SF36	LL	0.499	0.070	0.219	0.800
	XS	0.475	0.060	0.203	

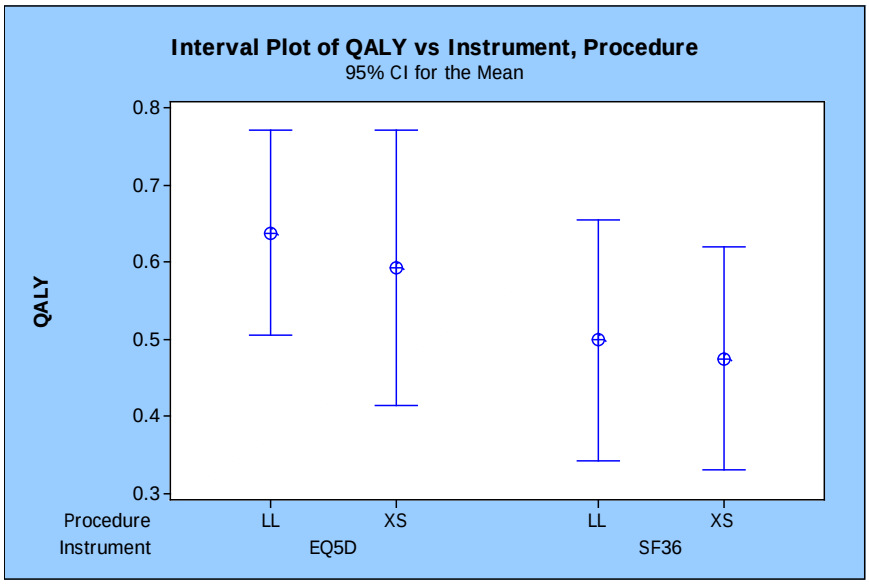
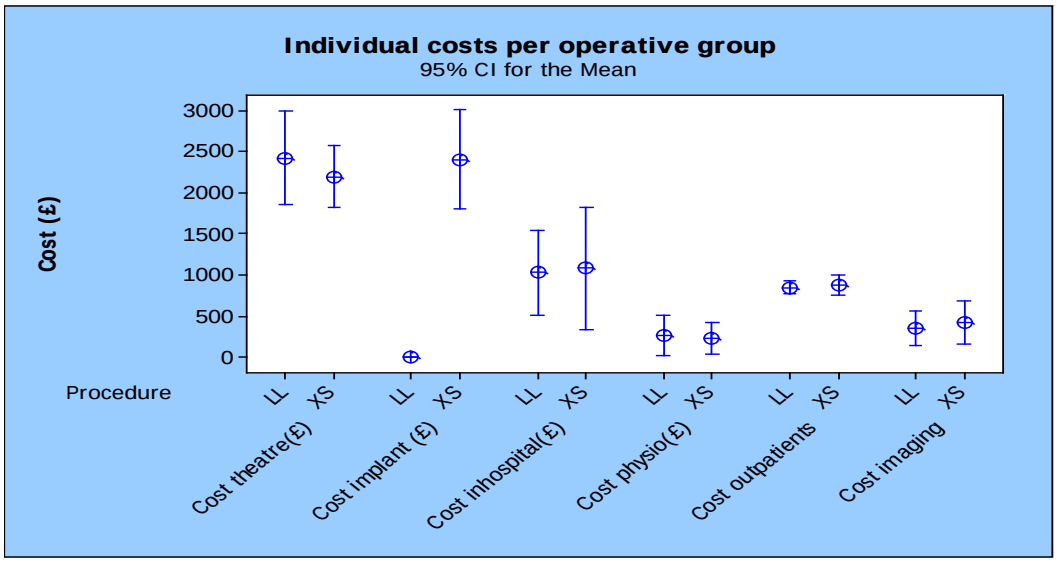


Figure 4.19: QALYs for both treatment groups (using EQ5D and SF36 instruments).

*4.4.2. **Costs***

While there is no significant difference in QALYs between the two treatment groups, the total cost was significantly greater in X-stop group (p=0.017) (Table 4.23).

The costs incurred for both procedures were comparable and non-significant for each component apart from the additional implant cost for the X-stop (Table 4.23, Figure 4.20A), regardless whether they were incurred in theatre, as inhospital stay, physiotherapy costs, outpatient clinics or imaging (Figure 4.20A).



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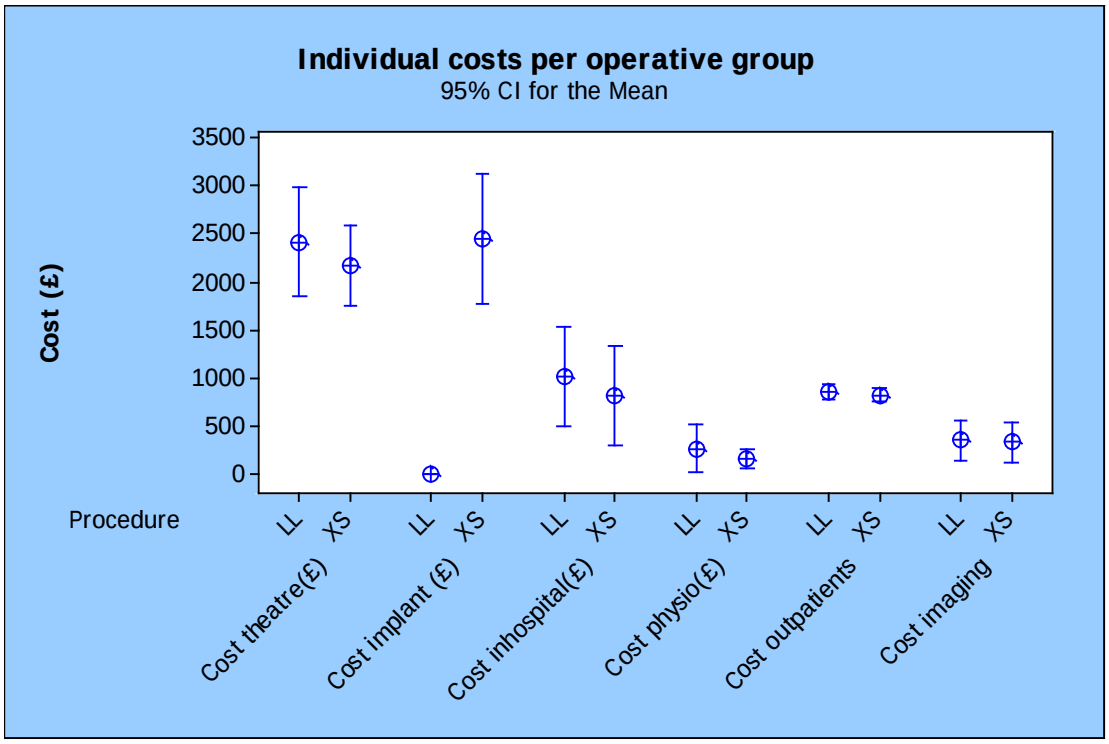


B)

Figure 4.20: Costs by treatment group (expressed as confidence intervals):

A) Outlier included; B) Outlier excluded.

Table 4.23: Costs incurred by theatre, implant, inhospital stay, physiotherapy inpatient sessions, outpatient clinics and imaging expenditure. The data analysed by Students t-test. A) Outlier included; B) Outlier excluded.
RED text indicates significant result.

	Procedure	Mean	SE	StDev	p-value
Cost theatre(£)	LL	2415.00	251.00	792.00	0.454
	XS	2184.00	166.00	526.00	
Cost implant(£)	LL	0.00	0.00	0.00	>0.05
	XS	2397.00	266.00	842.00	
Cost inhospital(£)	LL	1019.00	229.00	725.00	0.895
	XS	1073.00	329.00	1039.00	
Cost physio(£)	LL	257.00	108.00	342.00	0.829
	XS	226.50	85.00	268.70	
Cost outpatients(£)	LL	841.60	35.10	110.90	0.697
	XS	867.90	56.10	177.50	
Cost imaging(£)	LL	342.20	92.10	291.10	0.633
	XS	415.00	118.00	374.00	
Total cost (£)	LL	4874.00	535.00	1693.00	0.017
	XS	7162.00	674.00	2133.00	

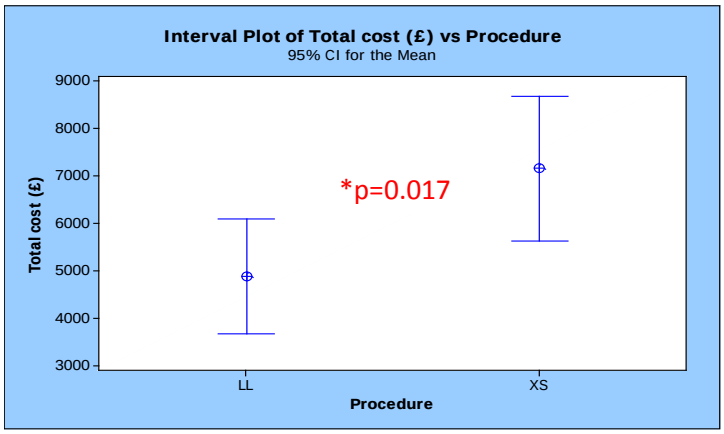
A)

	Procedure	Mean	SE	StDev	p-value
Cost theatre(£)	LL	2415.00	251.00	792.00	0.443
	XS	2165.00	185.00	554.00	
Cost implant (£)	LL	0.00	0.00	0.00	<0.05
	XS	2441.00	294.00	881.00	
Cost inhospital(£)	LL	1019.00	229.00	725.00	0.536
	XS	814.00	227.00	68.00	
Cost physio(£)	LL	257.00	108.00	342.00	0.396
	XS	151.00	43.60	130.80	
Cost outpatients	LL	841.60	35.10	110.90	0.620
	XS	818.20	29.20	87.70	
Cost imaging	LL	342.20	92.10	291.10	0.915
	XS	328.20	89.80	269.50	
Total cost (£)	LL	4874.00	535.00	1693.00	0.030
	XS	6718.00	568.00	1703.00	

B)

However, there was a significantly higher overall cost in X-stop group compared to Lumbar laminectomy group (p=0.017) (Figure 4.21A). Mean incremental cost for Lumbar laminectomy group was -£2288.60, with 95% CI for difference: (-4105.55, -471.65).

This difference in cost seems to arise from the additional cost of the implant since there was no significant difference in the cost for other areas of expenditure i.e. theatre costs, inhospital stay, physiotherapy sessions, outpatients and imaging (Table 4.23A, Figure 4.20A).



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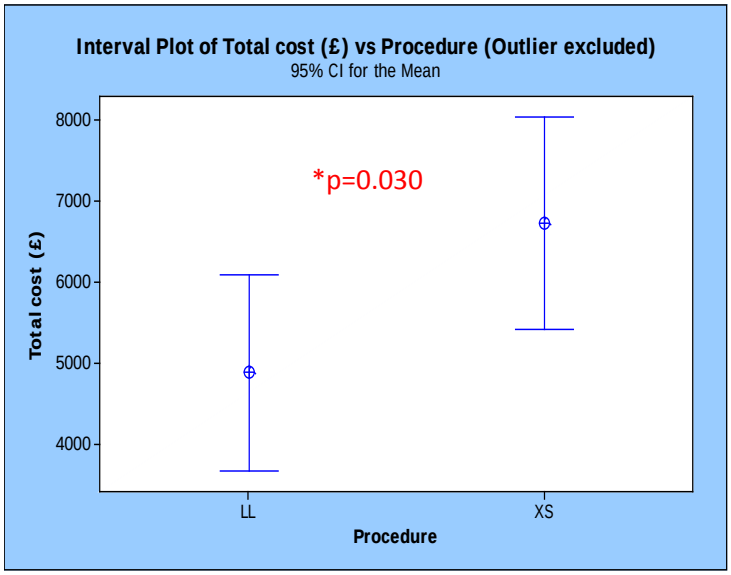


B)

Figure 4.21: Overall cost for Lumbar laminectomy and the X-stop group. Data shown as 95% CI of the mean.A) Outlier included, B)Outlier excluded. RED text indicates significant results.

4.4.3. **Incremental costs**

The incremental cost effectiveness ratio (ICER) per QALY gained of Lumbar laminectomy versus X-stop groups were:

- Using EQ5D: ICER = -£50919.4/QALY (=-£2288.581/0.0449QALY).

- Using SF36: ICER= -£94068.9/QALY (=-£2288.581/0.024QALY).

We have shown that the base-case effectiveness ratio with mean NHS cost gained of -£2288.581 in Lumbar laminectomy group yields 0.0449QALY (when EQ5D used) and 0.024QALY (when SF36 used) compared to the X-stop group.

Regardless of which one of two quality of life instruments is used to calculated QALYs, the base-case ratio in both situations is located in South East quadrant of cost effectiveness planes (Figure 4.22A and Figure 4.24A) suggesting that *Lumbar laminectomy is more cost-effective compared to the X-stop intervention.* This statement makes sense considering that our results have shown that Lumbar laminectomy is cheaper and yields greater QALYs compared to the X-stop group. However, this does not take into consideration any uncertainty in the estimates of costs and effects. Decision makers will be interested to ascertain how sure they can be that this is the correct conclusion to make.

The use of stochastic (bootstrapping) and probabilistic techniques (Monte Carlo simulation), for trial analyses and modelling studies respectively, we have generated 1000 sample data based on mean cost and efficacy (i.e. QALYs) from our study. This enables us to quantify the uncertainty surrounding the estimates of costs and effects. This is represented by the scatterplot of the incremental costs and QALYs in the cost-effectiveness plane.(161)

In order to decide if an intervention offers "good" value for money, the ICER must be compared to a specified monetary threshold. This threshold represents the maximum amount that the decision-maker is willing to pay for health effects (maximum acceptable ceiling ratio). The intervention is deemed cost-effective if the ICER falls below this threshold and not cost-effective otherwise.(162)

The suggested threshold acceptable ceiling ratio in technology appraisal for use in the NHS is about £30,000 per QALY gained as judged by the National Institute for Health and Clinical Excellence in England (167) Thus, the interpretation of the CELAX study is that, given a maximum acceptable ceiling ratio of £30,000 per QALY gained, the probability that Lumbar laminectomy is cost-effective compared to X-stop is 0.543 and 0.517 when EQ5D (Figure 4.23A) and SF36 (Figure 4.25A) used, respectively.

4.4.4. **Sensitivity Analysis**

One-level operations

When we compared 1-level Lumbar laminectomy versus X-stop we found again that Lumbar laminectomy group dominates:

ICER =-£25776/QALY (=-£2849.85/0.11QALYs)

We found that the cost gain in lumbar laminectomy group was -£2849.83 with 95% CI for difference: (-£4549.31, -£1150.36) (p=0.017) but with no significant difference in QALYs gained between the two groups (p=0.249).

Two-level operations

When we compared 2-level Lumbar laminectomy versus X-stop we found again that Lumbar laminectomy group dominates:

ICER =-£ -26348.5/QALY (=-£2890.96/0.11QALY).

There was no significant difference in cost (p=0.105) and QALYs(p=0.247) for two-level operations.

Costs with outlier excluded:

One of the participants who was randomised to the X-stop procedure continued to have ongoing pain postoperatively and stayed for 19 days in the hospital. Because of such a long inhospital stay this patient was considered as an 'Outlier' because of the suspected large impact on the costs. Postoperative MRI Lumbar spine of this patient showed an adequate decompression at the symptomatic level and no further stenosis. Patient subsequently had removal of X-stop and lumbar laminectomy which failed to improve symptoms. Further management included giving patient the option for spinal fusion or pain team follow up. Patient chose the latter. In view of the fact that following the X-stop procedure this patient had prolonged inhospital stay of 19 days because of ongoing back and leg pains but with evidence of satisfactory decompression on postoperative MRI Lumbar spine, we have reanalysed the cost and cost-effectiveness data to assess the impact on the costs with this Outlier excluded.

Even after excluding this patient no significant difference in mean inhospital stay was found (p=0.536) between two treatments and there was a persistent significance in lower cost of lumbar laminectomy compared to the X-stop (p=0.03)(Table 4.23B).

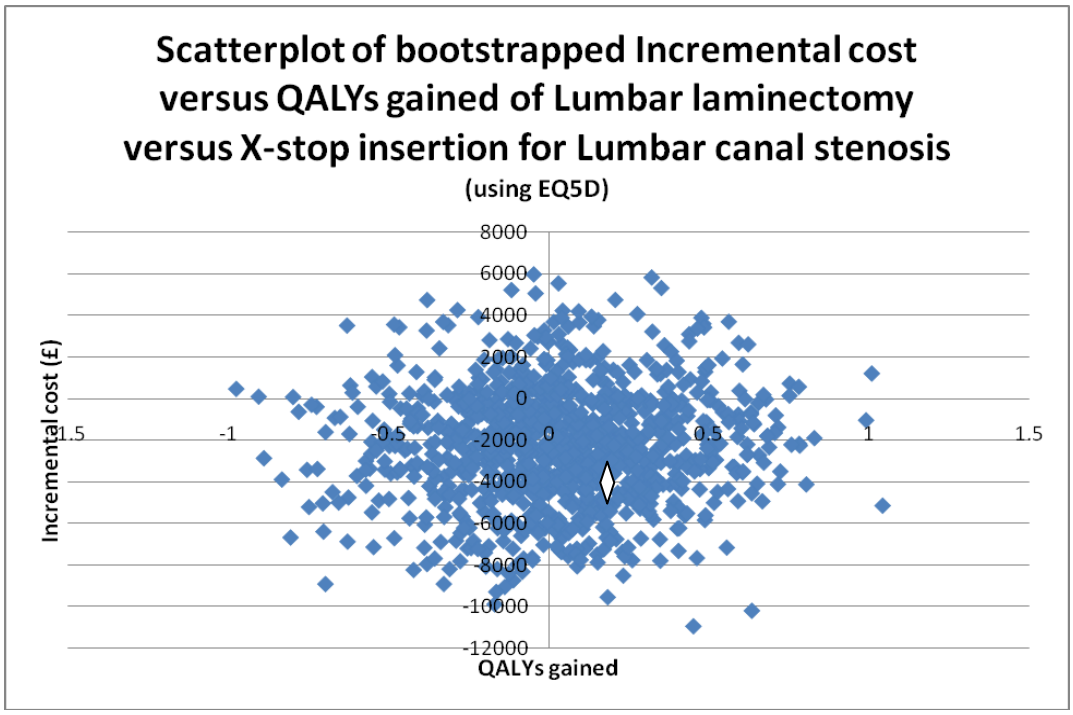
Cost-effectiveness data confirmed again that the base-case estimate was dominant:

- Using EQ5D: ICER = -£148785/QALY (=-£1844.60/0.012QALY) (Figure 4.22B)

- Using SF36: ICER= -£784680/QALY (=-£1844.60/0.002QALY) (Figure 4.24B):

again with low probability of the true effect in cost-effectiveness acceptability curve (Figure 4.23B and 4.25B).

Overall, exclusion of this outlier did not have any effect on the overall conclusions of the results.



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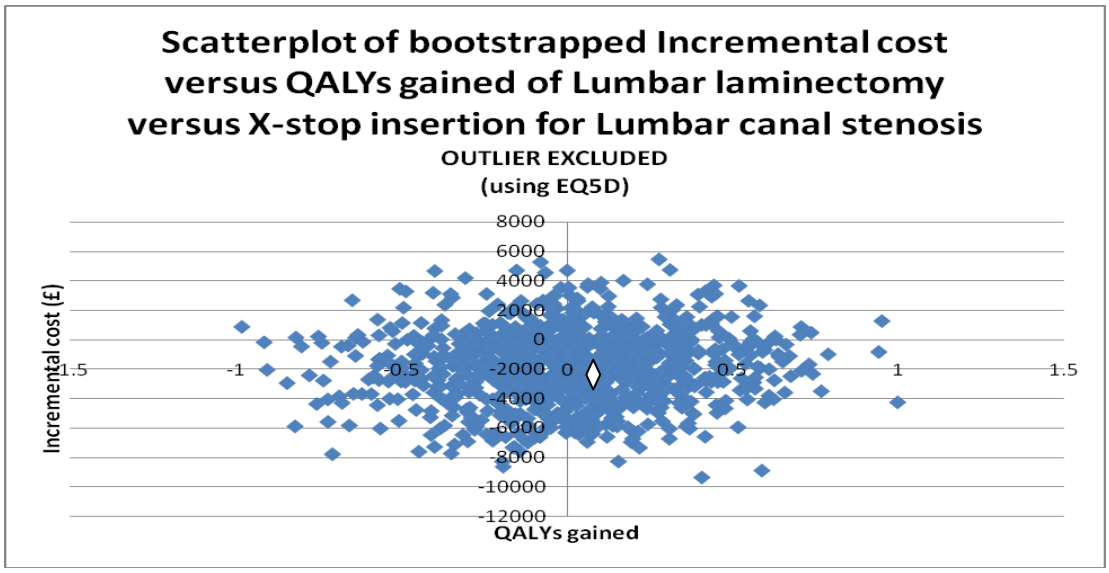
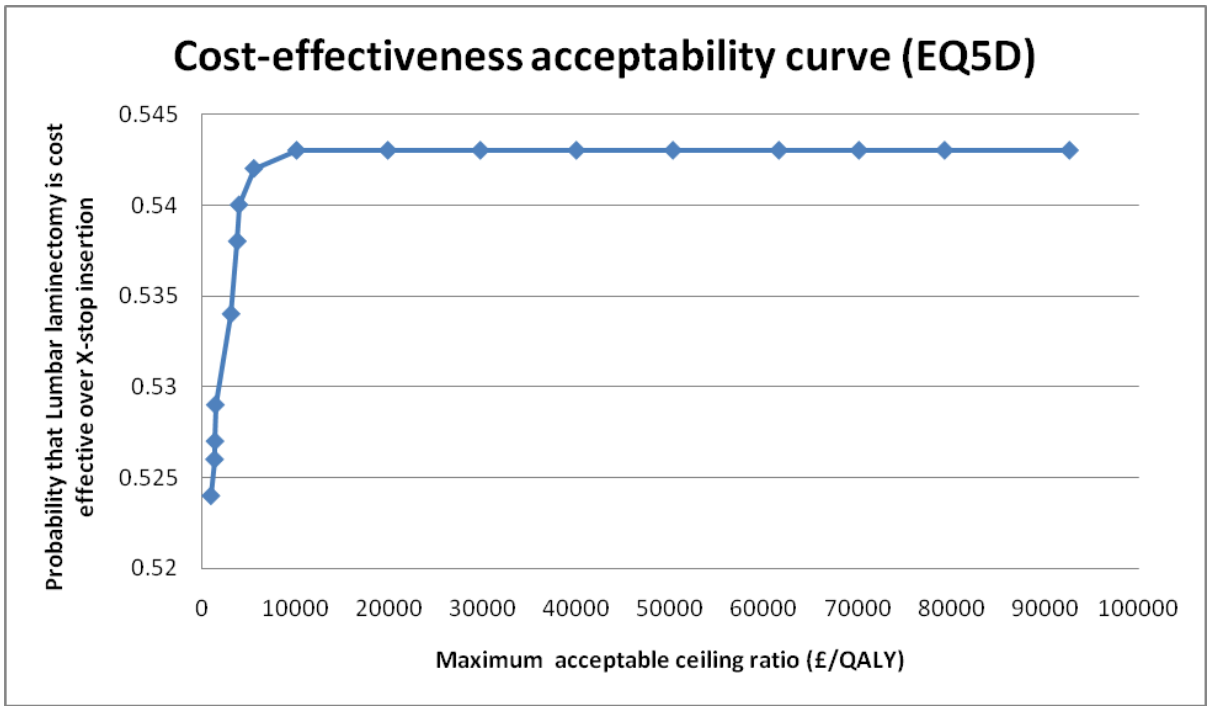


B)

Figure 4.22: The incremental cost effectiveness planed showing the scattered plots of bootstrapped incremental cost-effectiveness ratios of Lumbar laminectomy versus X-stop. A)Outlier included, B)Outlier excluded.

◊ Indicates base case estimates



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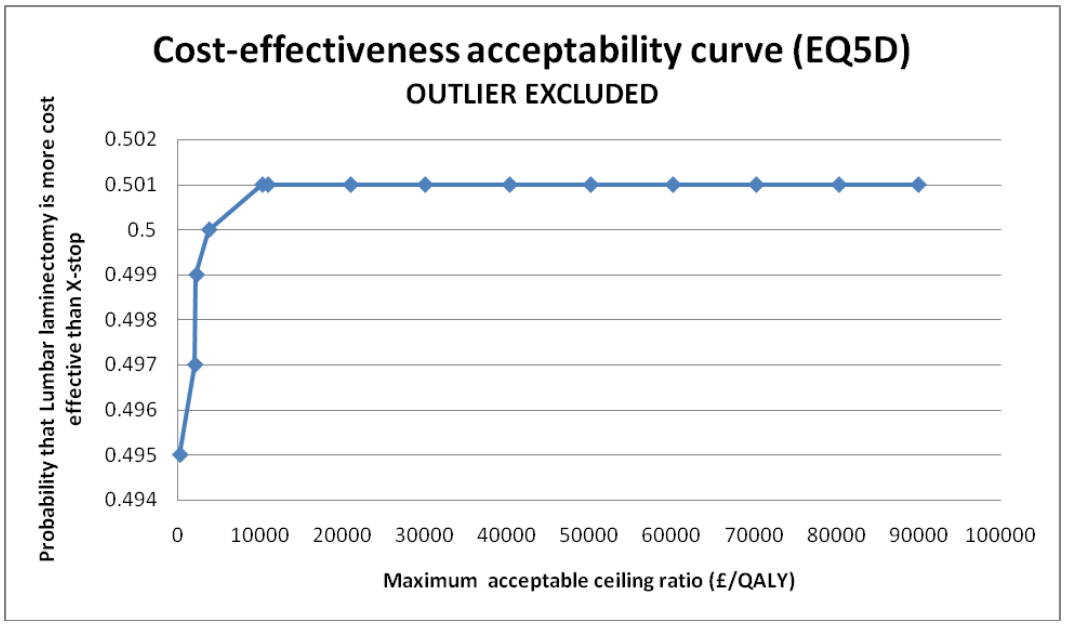
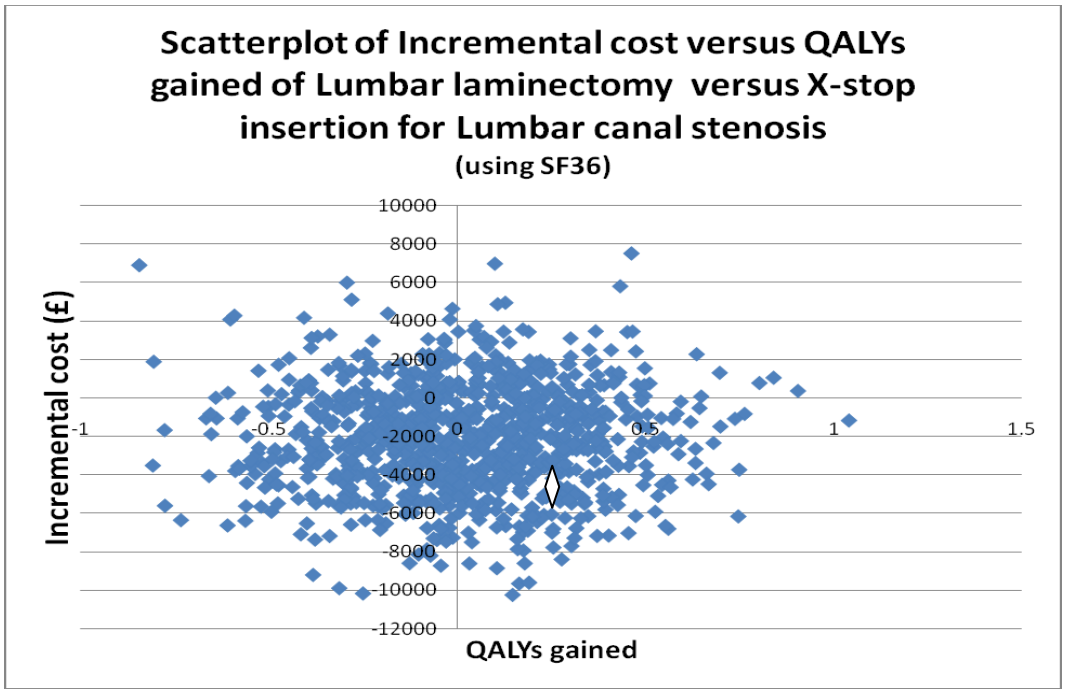
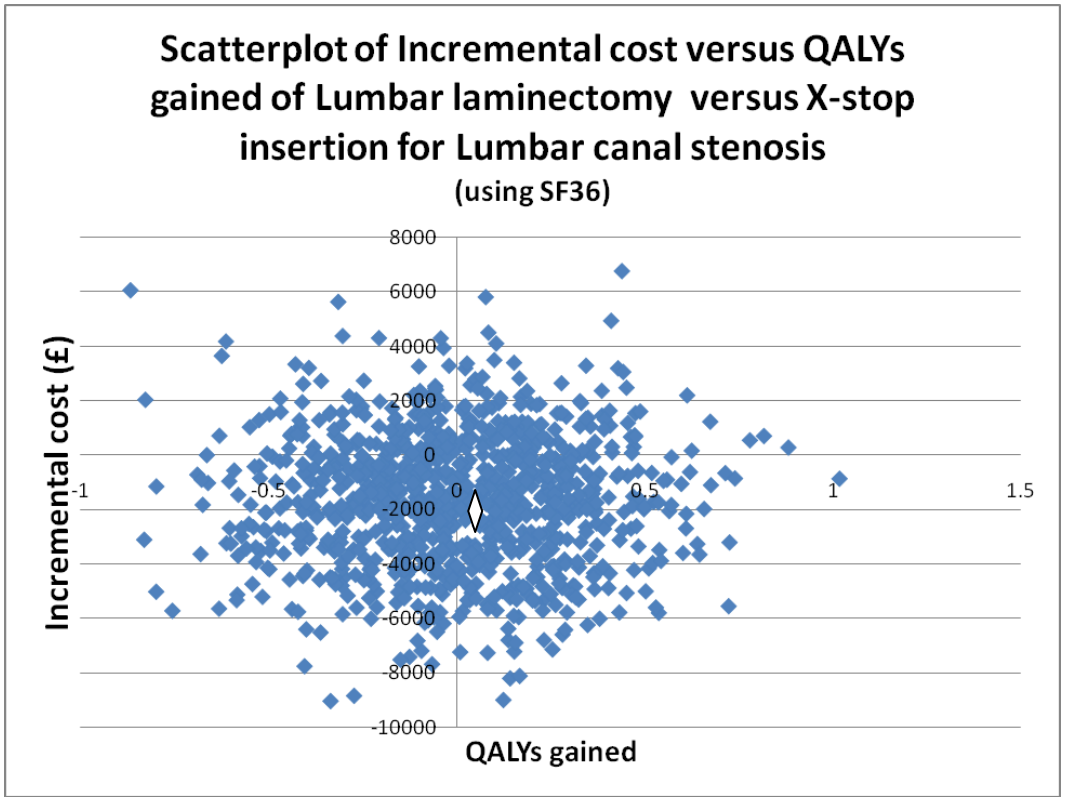


B)

Figure 4.23. Cost-effectiveness acceptability curves showing the probability that Lumbar laminectomy is cost-effective compared with X-stop using a range of cost-effectiveness thresholds. A)Outlier included, B)Outlier excluded.



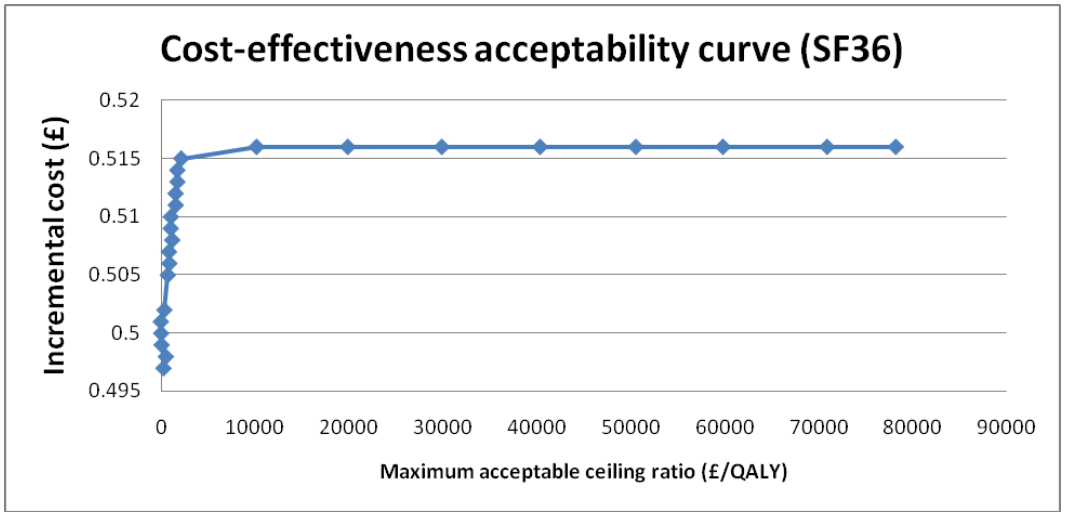
A)



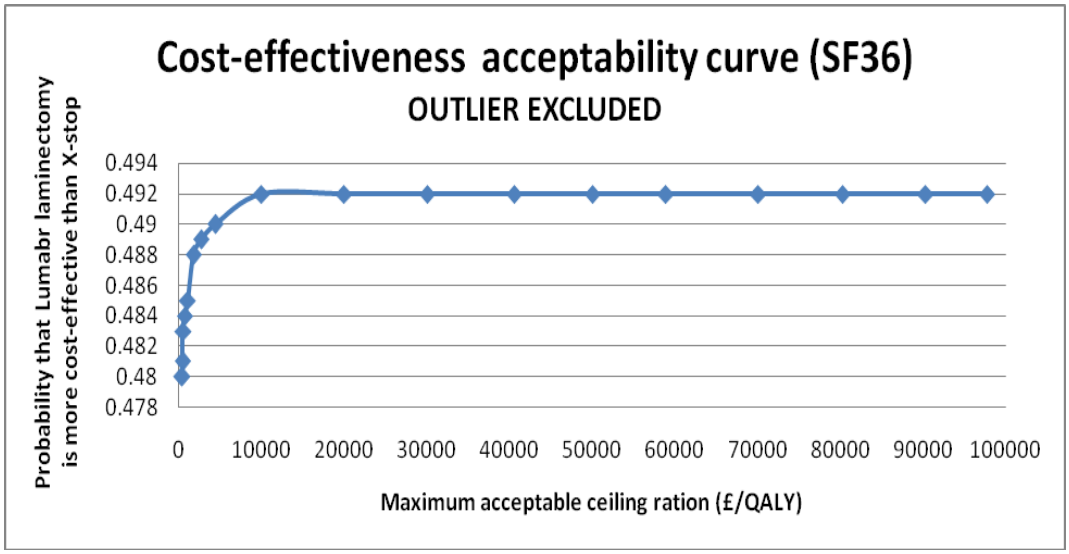
B)

Figure 4.24: Scattered plots of bootstrapped incremental cost-effectiveness ratios of Lumbar laminectomy versus X-stop. A) Outlier included, B) Outlier excluded.

◊ Indicates base case estimates



A)



B)

Figure 4.25. Cost-effectiveness acceptability curves showing the probability that Lumbar laminectomy is cost-effective compared with X-stop using a range of cost-effectiveness thresholds. A) Outlier included, B)Outlier excluded.

4.5. CLINICAL OUTCOMES

4.5.1. QBPDS and ODI

No significant difference (Table 4.24) were found in outcomes between two treatment groups for each period, as measured by QBPDS (Figure 4.26 and Table 4.25) and ODI (Figure 4.27, Table 4.26).

Table 4.24: p-values for clinical outcomes using different disease-specific instruments (QBPDS, ODI, ZCQ). Two-way factorial ANOVA performed on Period and Treatment groups. One-way ANOVA performed for each treatment groups.

	Two-way ANOVA		One-way ANOVA	
	Period	Treatment groups	Lumbar laminectomy	X-stop
QBPDS	0.640	0.385	0.807	0.303
ODI	0.466	0.203	0.834	0.546
ZCQ Symptom	0.001	0.760	0.069	0.042
ZCQ Physical	0.026	0.801	0.046	0.295
ZCQ Satisfaction	0.355	0.883	0.279	0.816

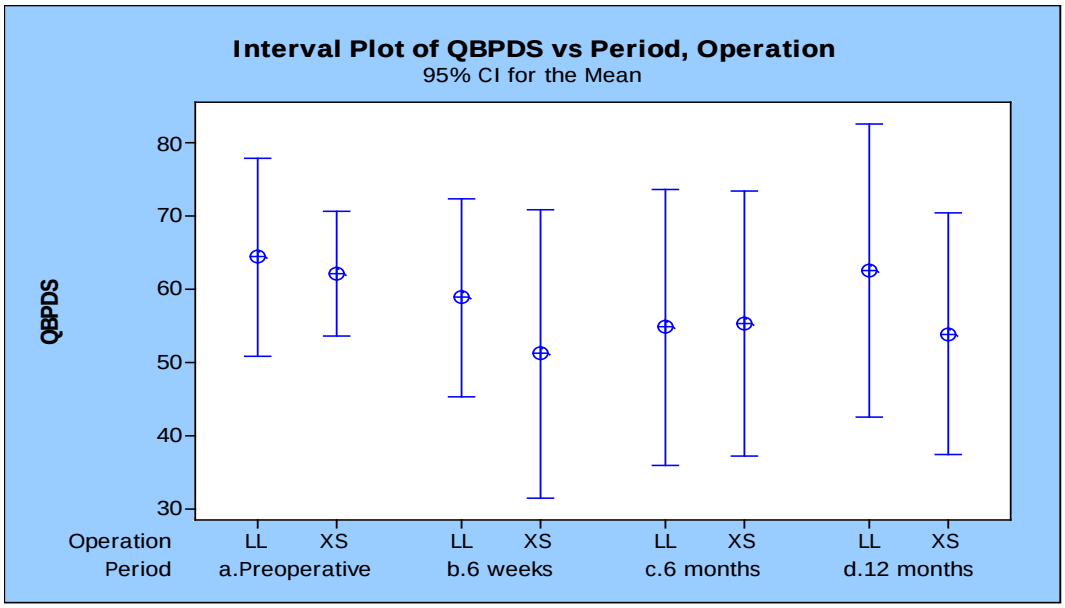


Figure 4.26: QBPDS confidence intervals for each Period for both treatment groups.

Table 4.25: QBPDS summary statistics, SE=Standard error of mean, StDev =Standard deviation.

	Procedure	Mean	SE	StDev
Preoperative				
	LL	64.38	6.00	18.98
	XS	62.10	3.81	12.06
6 weeks				
	LL	58.85	6.00	18.98
	XS	51.10	8.71	27.53
6 months				
	LL	54.75	8.40	26.55
	XS	55.25	8.03	25.40
12 months				
	LL	62.45	8.88	28.08
	XS	53.85	7.29	23.07

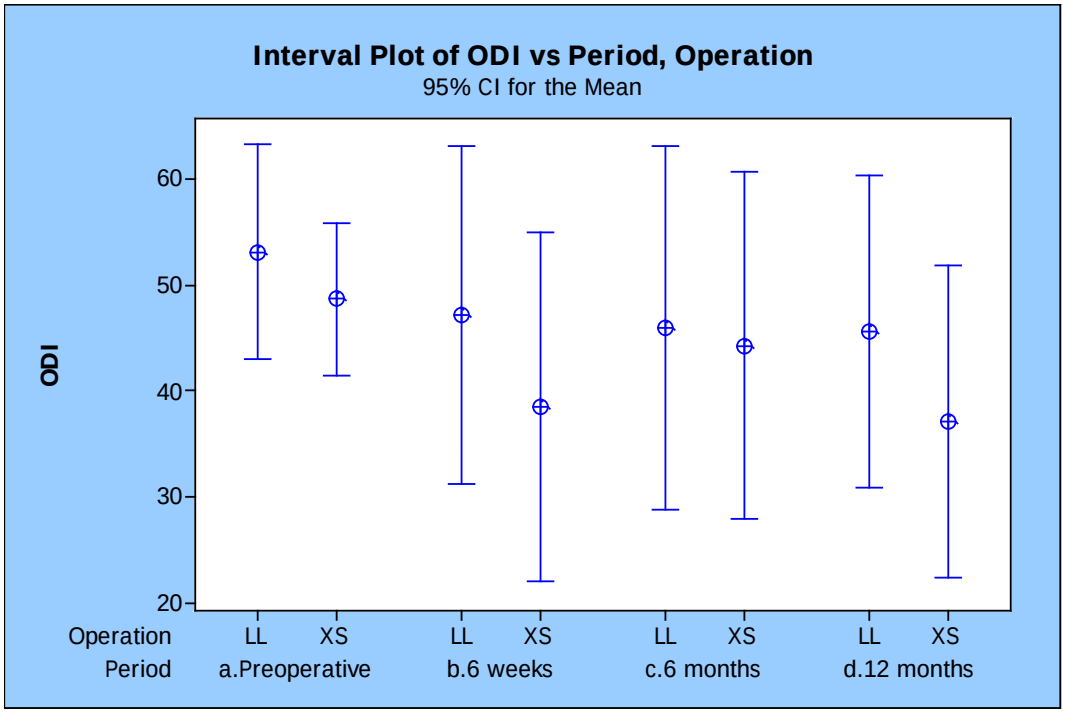


Figure 4.27: ODI confidence intervals for each Period for both treatment groups.

Table 4.26: ODI summary statistics, SE=Standard error of mean, StDev =Standard deviation.

	Procedure	Mean	SE	StDev
Preoperative				
	LL	53.11	4.49	14.19
	XS	48.67	3.17	10.02
6 weeks				
	LL	47.11	7.06	22.34
	XS	38.44	7.30	23.10
6 months				
	LL	46.00	7.60	24.05
	XS	44.22	7.25	22.94
12 months				
	LL	45.55	6.54	20.69
	XS	37.11	6.53	20.66

4.5.2. ZCQ

Two-way factorial ANOVA showed the following (Table 4.24):

- ZCQ Symptom component:- We found significant improvements in clinical outcomes between periods (p=0.001) but not between treatment groups(p=0.760).
- ZCQ Physical component: - There was a significant difference in clinical outcome between periods (p=0.026) but not between treatment groups (p=0.801).
- ZCQ Satisfaction scale:- There was no significant difference between periods(p=0.355) or treatment groups (p=0.883).

One –way ANOVA for different Periods in each treatment groups showed the following (Table 4.24):

- ZCQ Symptom component:- There was a significant improvement in X-stop group over different periods (p=0.042) but not in Lumbar laminectomy group (p=0.069).
- ZCQ Physical component:- There was a significant improvement in Lumbar laminectomy group (p=0.046) but not in X-stop group (p=0.295)
- ZCQ Satisfaction scale:- There was no significant difference in satisfaction scale between periods in Lumbar laminectomy (p=0.279) and X-stop group (0.816).

We found that there were significantly improved outcomes in ZCQ Symptom (Figure 4.28, Table 4.28) and Physical components (Figure 4.30, Table 4.30) noted for Lumbar laminectomy (Tables 4.27A) and X-stop groups (Table 4.27B) up to 12 months postoperatively when compared with preoperative period for each treatment groups (Student's t-test used).

Table 4.27: P-values of the difference between preoperative and other time periods using ZCQ Symptom and Physical component. in A) Lumbar laminectomy and B) X-stop groups.

Note: No Satisfaction component done as no preoperative values to compare it with. Also, Physical component at discharge not done in this study. RED values indicate significant p-values.

A) Lumbar laminectomy

	Symptom component	Physical component
Discharge	0.002	-
6 weeks	0.001	0.001
6 months	0.029	0.009
12 months	0.003	0.049

B) X-stop

	Symptom component	Physical component
Discharge	0.032	-
6 weeks	0.007	0.017
6 months	0.10	0.154
12 months	0.019	0.019

However, no significant results in improvement rates were found between two treatment groups for ZCQ Symptom component (Table 29, Figure 29) and ZCQ Physical component (Table 31, Figure 31) for each time period.

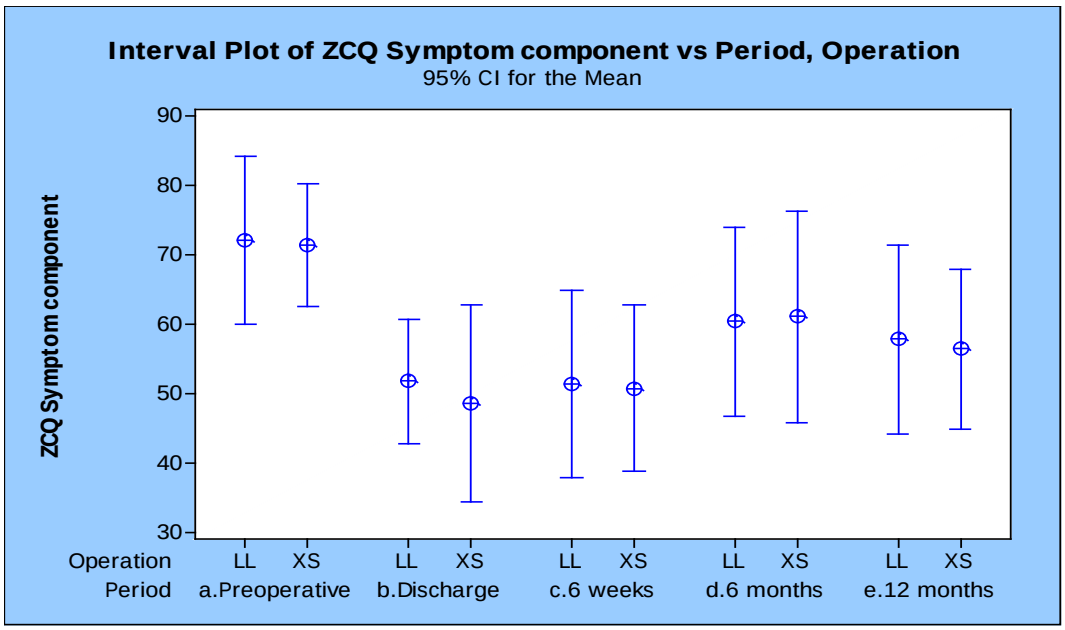


Figure 4.28: ZCQ Symptom component confidence intervals for each Period for both treatment groups.

Table 4.28: ZCQ Symptom component summary statistics, SE=Standard error of mean, StDev =Standard deviation. Values expressed as percentages.

	Procedure	Mean	SE	StDev
Preoperative				
	LL	72.14	5.32	16.82
	XS	71.43	3.91	12.37
Discharge				
	LL	51.78	3.96	12.51
	XS	48.57	6.28	19.86
6 weeks				
	LL	51.43	5.98	18.91
	XS	50.72	5.29	16.73
6 months				
	LL	60.36	6.01	19.01
	XS	61.07	6.77	21.39
12 months				
	LL	57.86	6.02	19.03
	XS	56.43	5.10	16.13

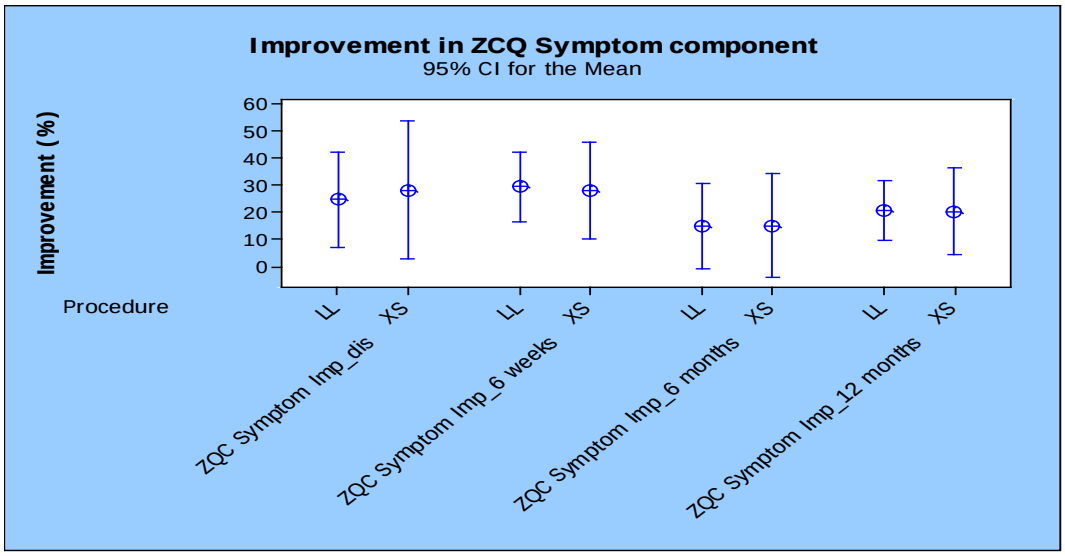


Figure 4.29: ZCQ Symptom component improvement rate confidence intervals for each Period for both treatment groups.

ZCQ Symptoms Imp_dis =Improvement rate at discharge

ZCQ Symptoms Imp_6 weeks =Improvement rate at 6 weeks

ZCQ Symptoms Imp_6 months =Improvement rate at 6 months

ZCQ Symptoms Imp_12 months =Improvement rate at 12 months

Improvement rate is calculated using the ZCQ Symptom component scores in formula:

Improvement rate = (Preop – postop scores)/preoperative scores*100%
Note that the higher the ZCQ score the worse is the outcome.

Table 4.29: ZCQ Symptom component improvement rate summary statistics, SE=Standard error of mean, StDev =Standard deviation. Values expressed as percentages.

Improvement rate = (Preop – postop)/preoperative *100%

	Procedure	Mean	SE	StDev	p-value
Discharge					
	LL	24.68	7.74	24.47	0.800
	XS	28.20	11.2	35.5	
6 weeks					
	LL	29.49	5.64	17.83	0.884
	XS	28.06	7.80	24.65	
6 months					
	LL	14.85	7.02	22.21	0.991
	XS	14.98	8.48	26.83	
12 months					
	LL	20.77	4.85	15.34	0.967
	XS	20.40	7.13	22.56	

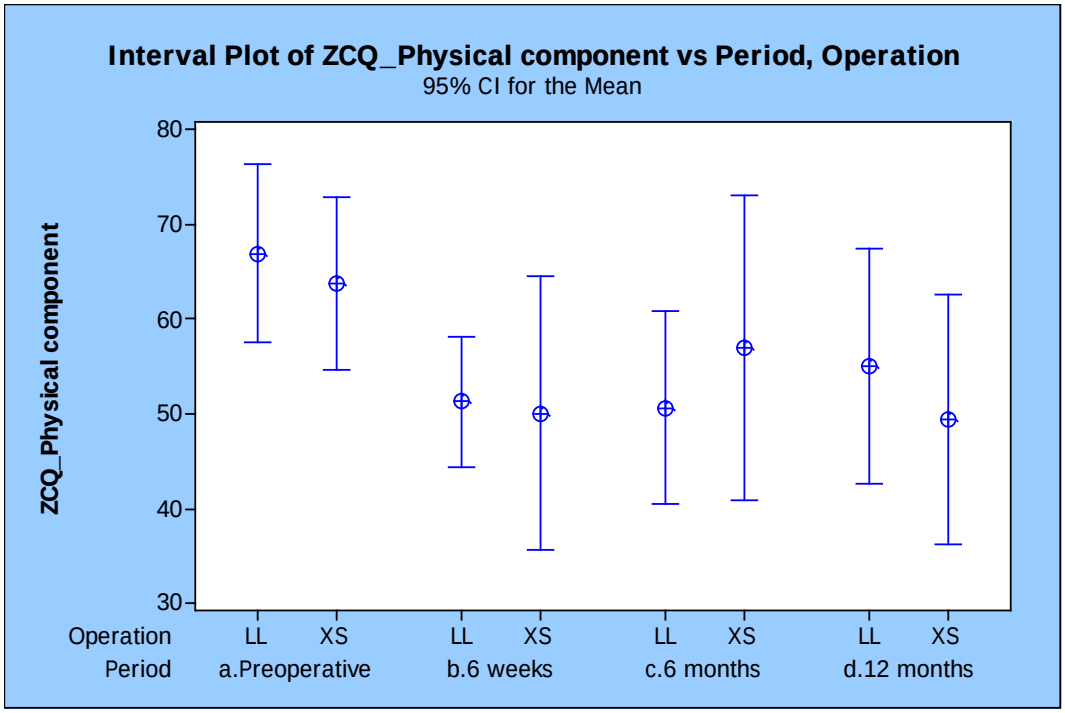


Figure 4.30: ZCQ Physical component confidence intervals for each Period for both treatment groups.

Table 4.30: ZCQ Physical component summary statistics, SE=Standard error of mean, StDev =Standard deviation. Values expressed as percentages.

	Procedure	Mean	SE	StDev
Preoperative				
	LL	66.88	4.17	13.19
	XS	63.75	4.04	12.77
6 weeks				
	LL	51.25	3.06	9.68
	XS	50.00	6.39	20.20
6 months				
	LL	50.63	4.51	14.27
	XS	56.88	7.12	22.53
12 **months**				
	LL	55.00	5.50	17.38
	XS	49.38	5.85	18.51

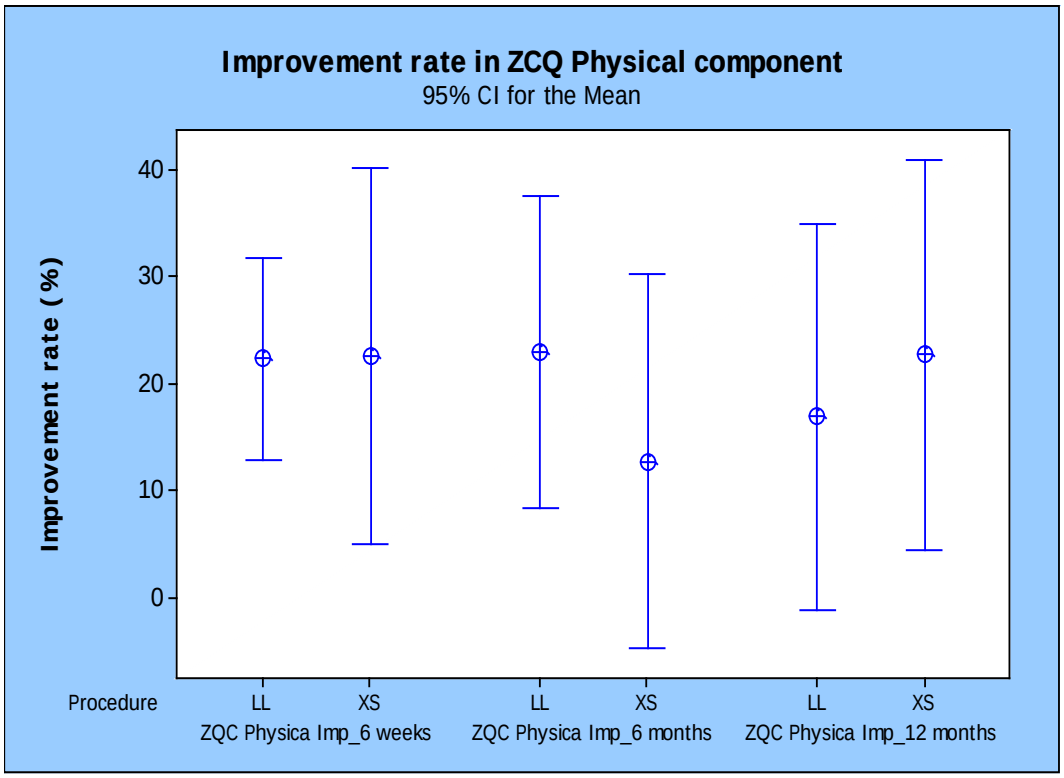


Figure 4.31: ZCQ Physical component improvement rate confidence intervals for each Period for both treatment groups.

ZCQ Physical Imp_dis =Improvement rate at discharge

ZCQ Physical Imp_6 weeks =Improvement rate at 6 weeks

ZCQ Physical Imp_6 months =Improvement rate at 6 months

ZCQ Physical Imp_12 months =Improvement rate at 12 months

Improvement rate is calculated using the ZCQ Physical component scores in formula:

Improvement rate = (Preop – postop scores)/preoperative scores*100%

Note that the higher the ZCQ score the worse is the outcome.

Table 4.31: ZCQ Physical component improvement rate summary statistics, SE=Standard error of mean, StDev =Standard deviation. Values expressed as percentages.

Improvement rate = (Preop – postop)/preoperative *100%

	Procedure	Mean	SE	StDev	p-value
6 weeks					
	LL	22.30	4.16	13.15	0.973
	XS	22.61	7.75	24.51	
6 months					
	LL	22.92	6.44	20.35	0.327
	XS	12.78	7.73	24.44	
12 months					
	LL	16.89	7.96	25.18	0.615
	XS	22.69	8.05	25.45	

It was not possible to compare the preoperative ZCQ satisfaction scores considering the obvious reason that satisfaction scores can only be obtained postoperatively. Descriptive summary of Satisfaction components are depicted in Table 32 and Figure 32).

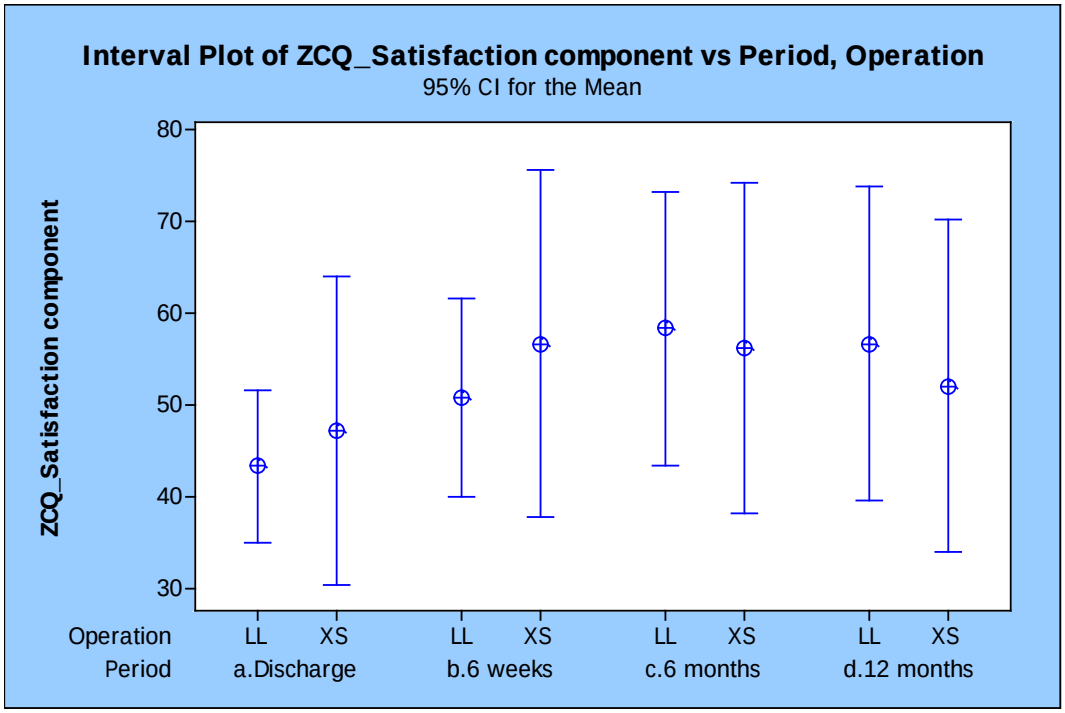


Figure 4.32: ZCQ Satisfaction component confidence intervals for each Period for both treatment groups.

Table 4.32: ZCQ Satisfaction component summary statistics, SE=Standard error of mean, StDev =Standard deviation. Values expressed as percentages.

	Procedure	Mean	SE	StDev
Discharge				
	LL	43.33	3.69	11.65
	XS	47.08	7.45	23.57
6 weeks				
	LL	50.83	4.80	15.19
	XS	56.67	8.38	26.51
6 months				
	LL	58.33	6.63	20.97
	XS	56.25	8.01	25.32
12 months				
	LL	56.67	7.59	23.99
	XS	52.08	8.06	25.48

4.5.3. **Success Rates**

The success rates of both lumbar laminectomy and X-stop groups were equal at 6 weeks of 50 % each followed by decreasing trend in both groups with 40% in Lumbar laminectomy and 30% in X-stop group. At 12 months period success rates of Lumbar laminectomy were 30 % while that of the X-stop was 60%. However, none of these success rates were significantly different from each other as their corresponding relative risks 95% confidence intervals include the indifference value of 1 (Table 4.33).

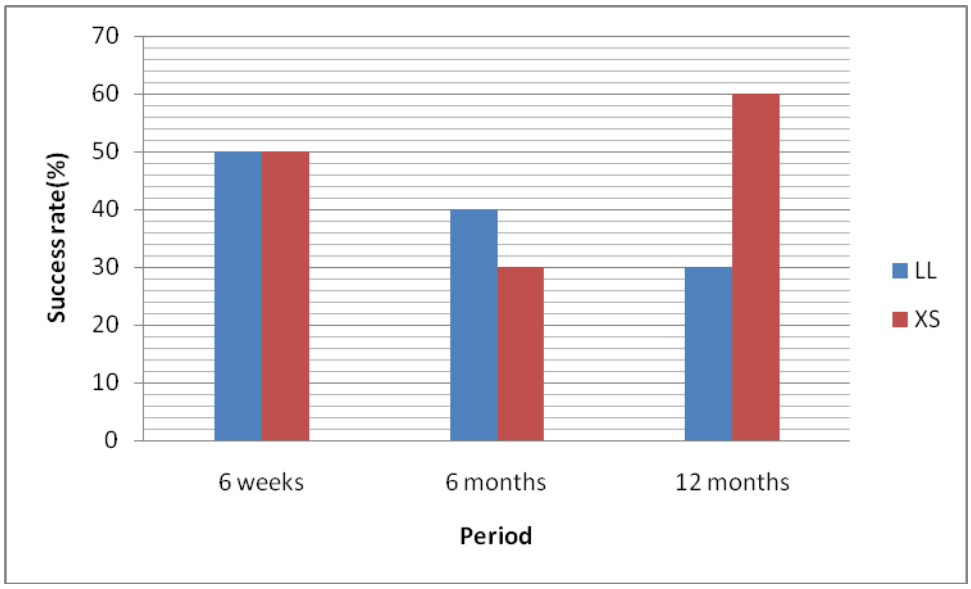


Figure 4.33: Success rate of the interventions. Success defined as ZCQ Symptom and Physical component more than 0.5 improvement in score and Satisfaction component <2.5. Data presented as percentage of successes

Table 4.33: Success rate of the interventions. Success defined as ZCQ Symptom and Physical component more than 0.5 improvement in score and Satisfaction component <2.5. Data presented as Counts(Percentage). Relative risks (RR) with 95% confidence intervals included.

	Success rate -Counts(Percentages)		
	6 weeks	**6 months**	**12 months**
LL	5(50)	4(40)	3(30)
XS	5(50)	3(30)	6(60)

$RR_{12\ months}$ =0.5 with 95% confidence interval is (0.17, 1.46)

$RR_{6\ months}$ =1.33 with 95% confidence interval is (0.396, 4.48)

$RR_{6\ weeks}$ =1.0 with 95% confidence interval is (0.416, 2.40)

4.6. **Predictor variables**

Using multivariate regression analysis techniques various proposed variables were analysed for the purpose of predictive values for costs, quality of life and clinical outcomes in our population group. Stepwise Regression methods were used to generate a more simplified model and yet to account for greater variance of data to explain the response variables analysed.

The explanatory variables chosen are the following:

- American Society of Anaesthesiology (ASA) score (levels 1 – 5)
- Actual level (the actual levels operated e.g. L2/3=2, L3/4=3, or L4/5=4, or L3/4, L4/5=34)

The values are the levels of the lumbar spine operated)

- Age
- BMI (Body Mass Index)
- Cobb angle
- Duration of symptom (months)
- Gender (Male =0; Female = 1)
- Levels (Variable 'Levels' takes only values 1 which means only one level operated and 2 means two levels operated)
- Procedure (Lumbar laminectomy = 0; X-stop =1)
- Smoking status (Non smoker = 0; Smoker = 1)
- Visual Analogue Scale (VAS)

Response variables used were:

- Cost
- EQ5D Score
- ODI
- QBPDS
- ZCQ Symptom component
- ZCQ Physical component
- ZCQ Satisfaction scale

at 12 months.

Table 4.34: Predictor factors for outcome measures below. (-) indicates NEGATIVE prediction; (+) indicates POSITIVE prediction; (0) indicates no prediction.

	ASA	**Actual level**	**Age**	**BMI**	**Duration of symptoms**	**Levels (number of levels operated)**	**Smoker**	**VAS (pain score)**
Cost	+	+	+	-	-	0	0	-
EQ5D	0	0	0	0	0	-	0	0
SF36								
BP	0	0	0	0	0	0	0	+
GH	0	-	0	0	0	0	0	0
MH	0	0	0	0	0	-	-	0
PF	0	0	0	0	0	-	0	0
RE	0	-	0	0	0	0	0	0
RP	0	-	0	0	0	0	0	0
SF	0	0	0	0	0	0	0	+
VT	0	0	0	0	0	0	0	0
QBPDS	0	0	0	0	0	+	0	0
ODI	0	0	0	0	0	0	0	0
ZCQ								
Symptom component	0	0	0	0	0	0	0	-
Physical component	+	+	0	-	0	0	0	0
Satisfaction component	0	0	0	0	0	0	0	0

4.6.1. **Cost**

We found that preoperative higher ASA score, older age, lower BMI, higher actual levels operated (e.g. L3/4 is higher level than L4/5), shorter the duration of symptoms and lower preoperative VAS score for pain were associated with higher costs.

Regression model for Cost is as follows:
Total Cost (£) = 5757+1793 x ASA +171.6 x Age -359.7 x BMI +156.4 x Actual levels -13.29 x Duration of symptoms – 674 x VAS.

4.6.2. **Quality of life**

EQ5D score: - It is found that only Levels variable (number of levels operated) was associated with worse quality of life as measured by EQ5D score.
Regression model for EQ5D score is: EQ5D score = 1.168 – 0.561 x Levels.

SF36 domains:

Bodily pain (BP): - VAS score were negatively associated with BP score. Regression model is: BP= -10.8 + 7.88 x VAS.

General Health (GH):- It is found that only 'Actual levels' variable was associated with worse GH score. This means that the lower the level where decompression takes place, the worse the GH domain score. This is because the lower levels operated take higher values and that the Actual level has negative predictive values (as shown in regression equation). Regression model is:
GH = 63.59 – 0.924 x Actual level.

Mental Health (MH):- It is found that number of levels operated and people who smoke have worse MH score. Regression model is:
MH = 118.9-26.68 x Levels -15.92 x Smoker

Physical Functioning (PF): -Higher the number of levels operated, is associated with worse PF score. Regression model is: PF = 79.1 – 30.6 x Levels

Role Emotional (RE):- The lower the actual levels are operated the worse the Role Emotional score is predicted. Regression model is: RE = 76.3 – 1.686 x Actual level

Role Physical (RP):- The lower the actual levels are operated the worse the Role Physical score is predicted. Regression model is: RE = 58.4 – 1.99 x Actual level

Social Functioning (SF):- Higher VAS score pain, is associated with worse SF score. Regression model is: SF =-11.5 + 9.51 x VAS

Vitality (VT):- No predictor variables were found for VT score.

4.6.3. **Clinical outcomes**

- *QBPDS:*- Higher the number of levels operated, is associated with higher (worse) QBPDS score. Regression model is: QBPDS = 45.92 +1.172 x Levels.

- *ODI:*- Interestingly no predictors were found for the ODI score.

- *ZCQ Symptom component:*- Higher the number of levels operated, is associated with higher (worse) ZCQ Symptom component score.
  Regression model is:
  ZCQ Symptom component = 93.4 – 5.1 x VAS

- *ZCQ Physical component:*- Higher ASA score, lower segmental levels operated and higher the BMI have negative predictive values on ZCQ Physical component. Regression analysis model is:

ZCQ Physical component = 86.7 +17.01 x ASA +1.038X Actual level – 2.806 x BMI

- *ZCQ Satisfaction component:-* No variables were found to be significant predictors at 12 months.

- *Success rates:-* Logistic binary regression for Success of treatment (defined as at least response 'somewhat satisfied' and ZCQ Symptom and Physical component improvement of greater than 0.5) then the POSITIVE predictive factor to success is:- higher BMI, while the NEGATIVE predictors to success are: - higher ASA score, the lower the operated levels and longer the duration of symptoms preoperatively.
  Regression analysis model is:
  Logit (p) = -152 - 49 x ASA -3.0 x Actual level +11 x BMI -0.83 x Duration of symptoms.

4.7. RADIOLOGICAL DATA

There were no significant differences in baseline radiological features between Lumbar laminectomy and X-stop group (Table 4.35).

Table 4.35: Radiological preoperative data summary for two treatment groups. SE=Standard error of mean, StDev =Standard deviation. Number of patients in Lumbar laminectomy group were 9 while in X-stop group were 10.

	Operation	Mean	SE	StDev	p-value
Spinal canal area (mm^2)	LL	89.7	17.5	52.6	0.121
	XS	54.8	12.8	40.5	
Interspinous distance (mm)	LL	5.9	0.8	2.6	0.071
	XS	3.8	0.7	2.1	
Foramen area(mm^2)	LL	69.6	9.3	27.9	0.396
	XS	58.3	9.0	28.5	
Anterior disc height(mm)	LL	9.7	1.3	3.8	0.671
	XS	9.0	1.2	3.7	
Posterior Disc Height (mm)	LL	5.6	0.6	1.9	0.740
	XS	5.3	0.9	2.8	
Size of ligamentum flavum (mm)	LL	5.2	0.7	2.1	0.745
	XS	4.8	0.8	2.4	
Average facet size(mm)	LL	17.8	0.7	2.0	0.184
	XS	15.8	1.3	4.0	
Size of posterior disc bulge (mm)	LL	3.7	0.5	1.6	0.720
	XS	4.1	1.0	3.1	
Intervertebral angle (degree)	LL	6.0	1.0	3.0	0.149
	XS	3.9	0.9	2.9	
Cobb angle (degree)	LL	12.3	2.7	8.2	0.106
	XS	5.6	2.8	8.9	

4.8. BIOMECHANICAL ANALYSIS

Further analysis of biomechanical features were done. In view of small number of patients who have had preoperative and postoperative MRI Lumbar spine, we have used nonparametric statistical tests to analyse the results.

The analysis was done AT THE OPERATIVE LEVEL and ADJACENT LEVELS.

4.8.1. **Operative level**

Our analysis showed that:

4.8.1.1. *Spinal canal area:-* There was no significant difference in the change of the spinal canal area between the two treatment groups (p=0.136) (Figure 4.34 and Table 4.36). In addition, there were no significant differences between preoperative and postoperative spinal canal area in Lumbar laminectomy (p=0.144) and X-stop (p=1.0).

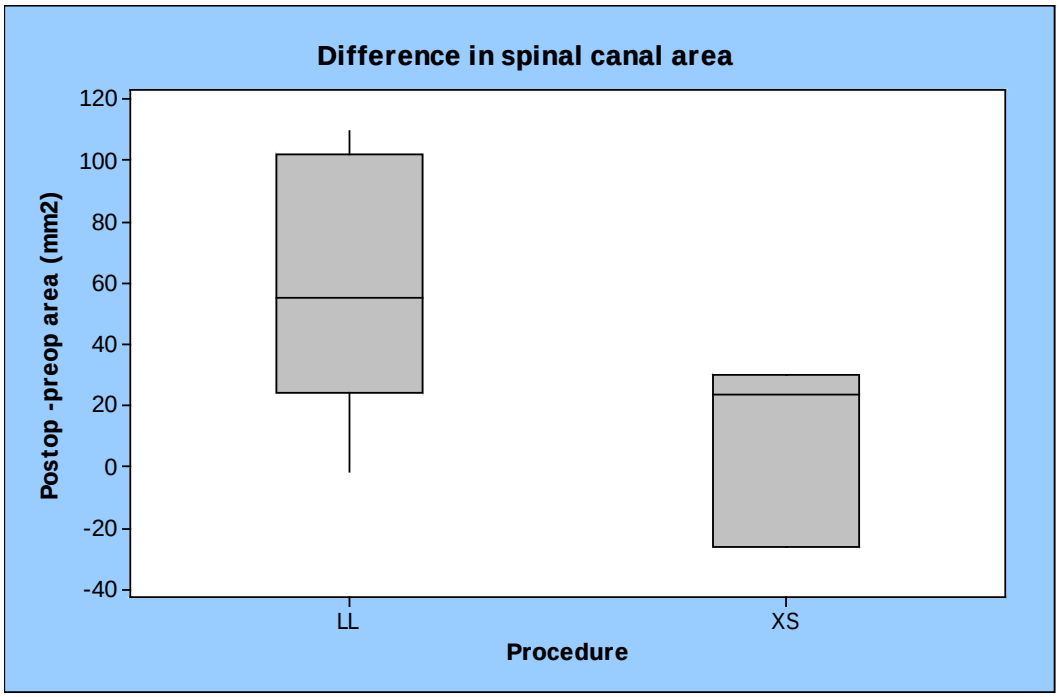


Figure 4.34: Boxplot of change of preoperative and postoperative spinal canal area for two treatment groups.

Table 4.36: Preoperative, postoperative and change in spinal canal area(mm^2). IQR=Interquartile range.

	Procedure	Number of patients	Median	IQR	p-value
Preoperative	LL	5	75.5	93.7	-
	XS	3	55.7	78.9	
Postoperative	LL	5	152.2	51.2	-
	XS	3	79.5	135.4	
Change in spinal canal area (mm^2)	LL	5	55.0	78.2	0.136
	XS	3	23.8	56.5	

4.8.1.2. *Foramen canal area:-* There was no significant difference in the change of the intervertebral foramen area between the two treatment groups (p=0.767) (Figure 4.35 and Table 4.37). Also, there were no significant differences between preoperative and postoperative intervertebral foramen in Lumbar laminectomy (p=1.0) and X-stop (p=1.0).

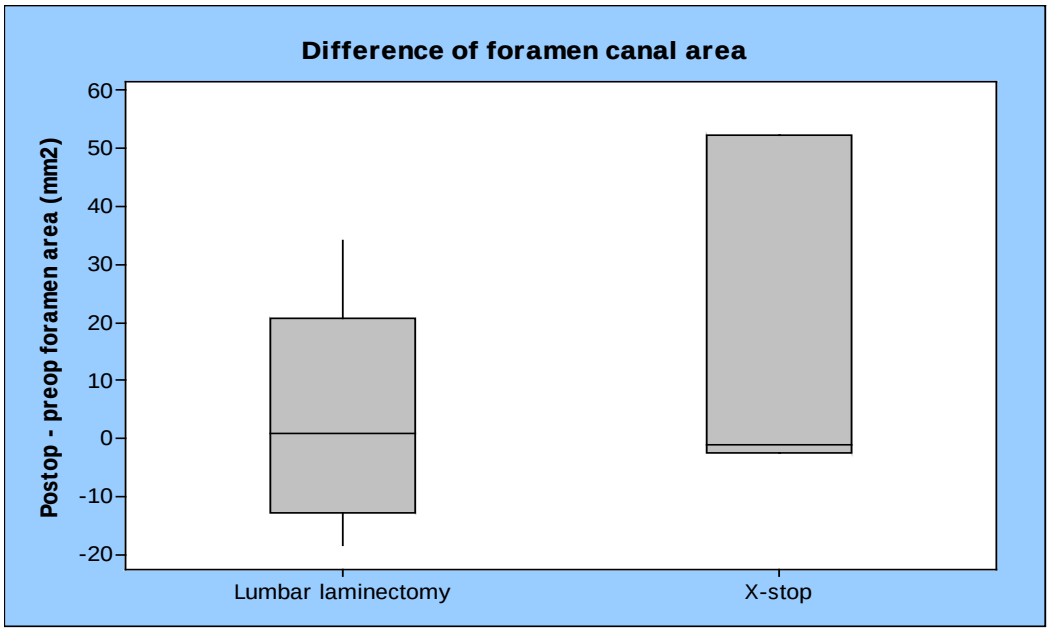


Figure 4.35: Boxplot of change of preoperative and postoperative foramen area for two treatment groups.

Table 4.37: Preoperative, postoperative and change in foramen area(mm^2). IQR=Interquartile range.

	Procedure	Number of patients	Median	IQR	p-value
Preoperative	LL	5	82.0	61.2	-
	XS	3	54.2	76.4	
Postoperative	LL	5	76.0	37.5	-
	XS	3	68.0	36.1	
Change in foramen area (mm^2)	LL	5	0.9	33.8	0.767
	XS	3	-0.9	55.1	

4.8.1.3. *Anterior disc height:-* There was no significant difference in the change of the anterior disc height between the two treatment groups (p=1.0) (Figure 4.36 and Table 4.38). In addition, there were no significant differences between preoperative and postoperative anterior disc height in Lumbar laminectomy (p=0.917) and X-stop (p=1.0).

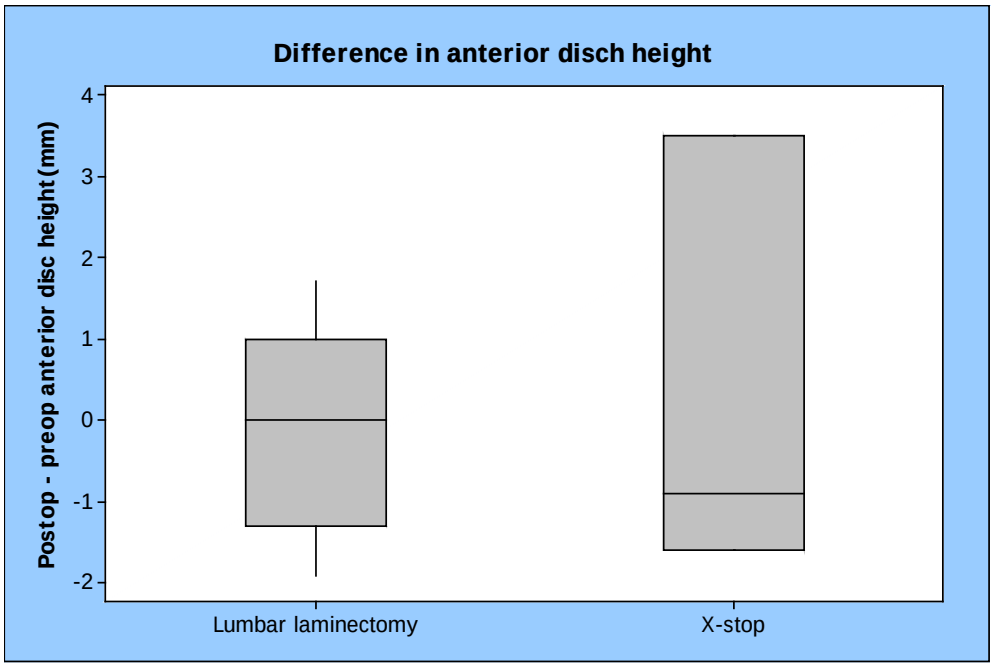


Figure 4.36: Boxplot of change of preoperative and postoperative anterior disc height for two treatment groups.

Table 4.38: Preoperative, postoperative and change in anterior disc height(mm). IQR=Interquartile range.

	Procedure	Number of patients	Median	IQR	p-value
Preoperative	LL	5	9.4	4.3	-
	XS	3	9.5	1.7	
Postoperative	LL	5	9.1	3.7	-
	XS	3	10.2	5.0	
Change in anterior disc height (mm)	LL	5	0.0	2.3	1.0
	XS	3	-0.9	5.1	

4.8.1.4. *Posterior disc height*: - There was no significant difference in the change of the posterior disc height between the two treatment groups (p=0.551) (Figure 4.37 and Table 4.39). Also, there were no significant differences between preoperative and postoperative posterior disc height in Lumbar laminectomy (p=0.531) and X-stop (p=1.0).

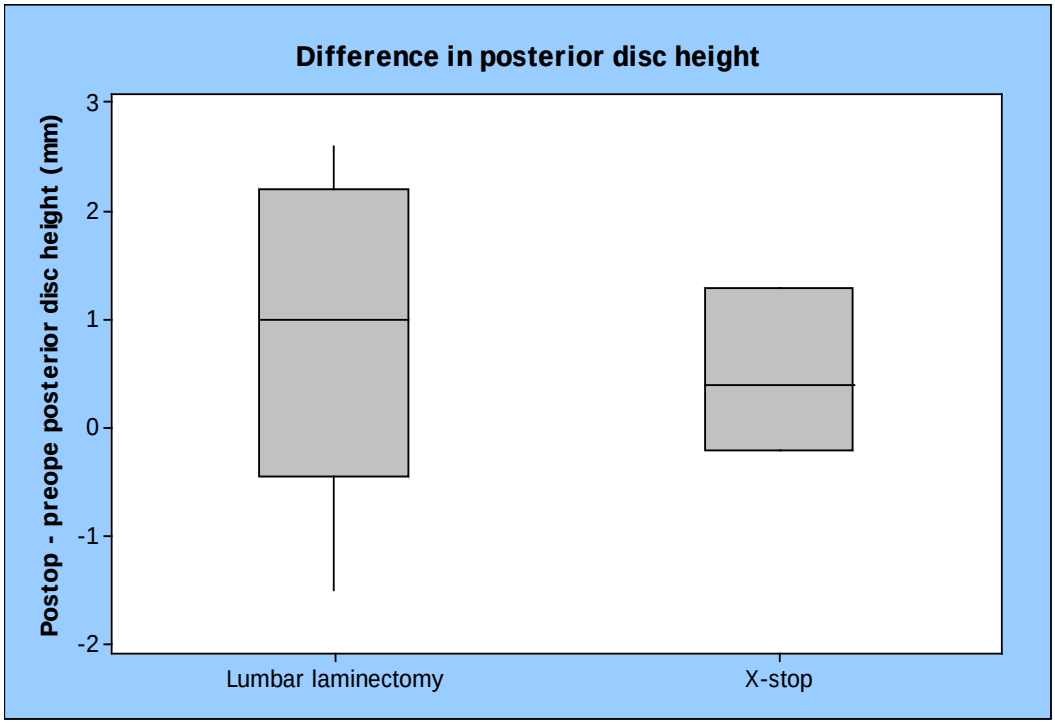


Figure 4.37: Boxplot of change of preoperative and postoperative posterior disc height for two treatment groups.

Table 4.39: Preoperative, postoperative and change in posterior disc height(mm). IQR=Interquartile range.

	Procedure	Number of patients	Median	IQR	p-value
Preoperative	LL	5	5.7	2.4	-
	XS	3	5.0	5.5	
Postoperative	LL	5	6.0	4.1	-
	XS	3	4.8	4.6	
Change in posterior disc height (mm)	LL	5	1.0	2.6	0.551
	XS	3	0.4	1.5	

4.8.1.5. *Facet joint size:* - There was no significant difference in the change of the facet joint size between the two treatment groups (p=0.551) (Figure 4.38 and Table 4.40). Also, there were no significant differences between preoperative and postoperative facet joint size in Lumbar laminectomy (p=0.144) and X-stop (p=1.0).

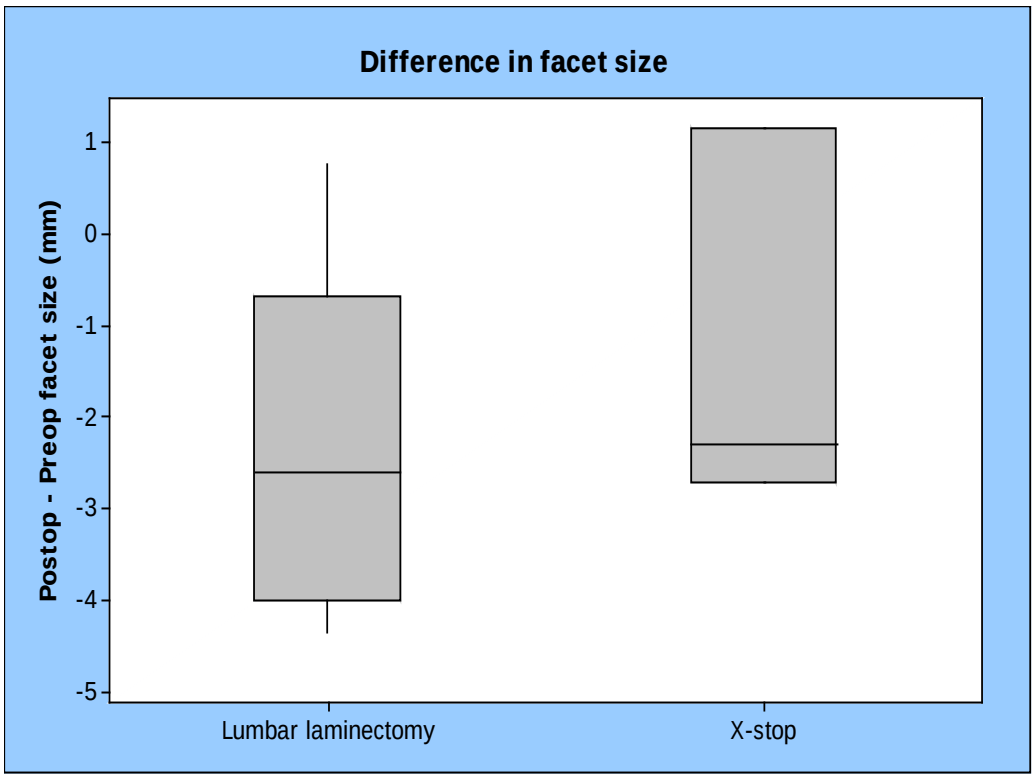


Figure 4.38: Boxplot of change of preoperative and postoperative facet size for two treatment groups.

Table 4.40: Preoperative, postoperative and change in facet size(mm). IQR=Interquartile range.

	Procedure	Number of patients	Median	IQR	p-value
Preoperative	LL	5	16.6	2.6	-
	XS	3	15.5	5.7	
Postoperative	LL	5	13.0	5.4	-
	XS	3	13.6	2.3	
Change in facet joint size (mm)	LL	5	-2.6	3.3	0.551
	XS	3	-2.3	3.8	

4.8.1.6. *Intervertebral angle:* - There was no significant difference in the change of the facet joint size between the two treatment groups (p=0.767) (Figure 4.39 and Table 4.41). Also, there were no significant differences between preoperative and postoperative intervertebral angle in Lumbar laminectomy (p=0.834) and X-stop (p=0.383).

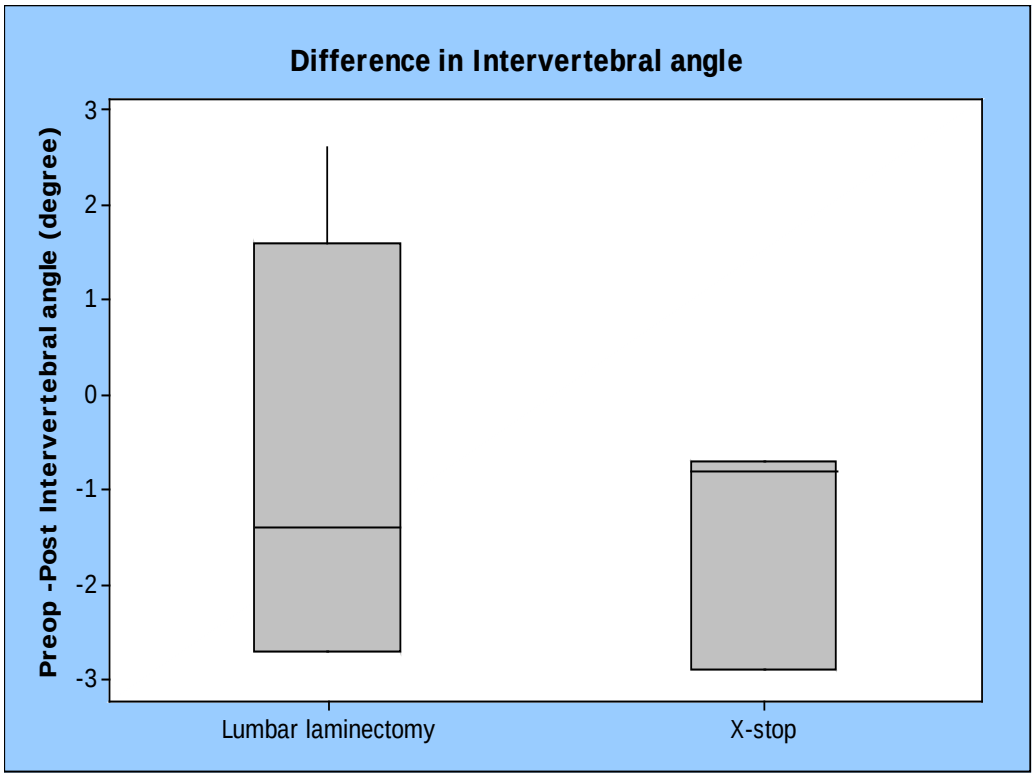


Figure 4.39: Boxplot of change of preoperative and postoperative Intervertebral angles for two treatment groups.

Table 4.41: Preoperative, postoperative and change in Intervertebral angles (degrees). IQR=Interquartile range.

	Procedure	Number of patients	Median	IQR	p-value
Preoperative	LL	5	8.2	4.5	-
	XS	3	5.4	1.5	
Postoperative	LL	5	5.5	4.9	-
	XS	3	4.2	3.3	
Change in intervertebral angle (degree)	LL	5	-1.4	4.3	0.767
	XS	3	-0.8	2.2	

4.8.1.7. *Posterior disc bulge:* - There was no significant difference in the change of the posterior disc bulge between the two treatment groups (p=1.0) (Figure 4.40 and Table 4.42). Also, there were no significant differences between preoperative and postoperative posterior disc bulge in Lumbar laminectomy (p= 1.0) and X-stop (p=1.0).

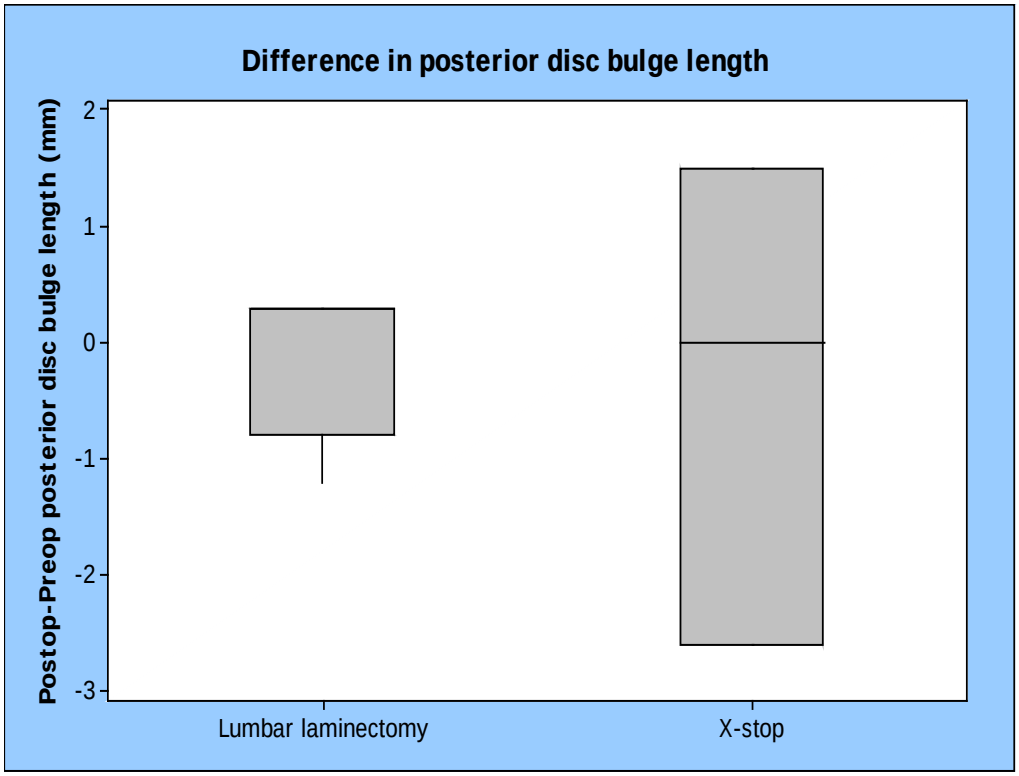


Figure 4.40: Boxplot of change of preoperative and postoperative posterior disc bulge for two treatment groups.

Table 4.42: Preoperative, postoperative and change in posterior disc bulge (mm). IQR=Interquartile range.

	Procedure	Number of patients	Median	IQR	p-value
Preoperative	LL	5	4.1	1.5	-
	XS	3	4.0	8.5	
Postoperative	LL	5	4.2	1.8	-
	XS	3	5.5	5.9	
Change in posterior disc bulge (mm)	LL	5	0.3	1.1	1.0
	XS	3	0.0	4.1	

4.8.1.8. *Cobb angle:-* There was no significant difference in the change of the Cobb angle between the two treatment groups (p=0.881) (Figure 4.41 and Table 4.43). Also, there were no significant differences between preoperative and postoperative Cobb angle in Lumbar laminectomy (p=0.917) and X-stop (p=1.0).

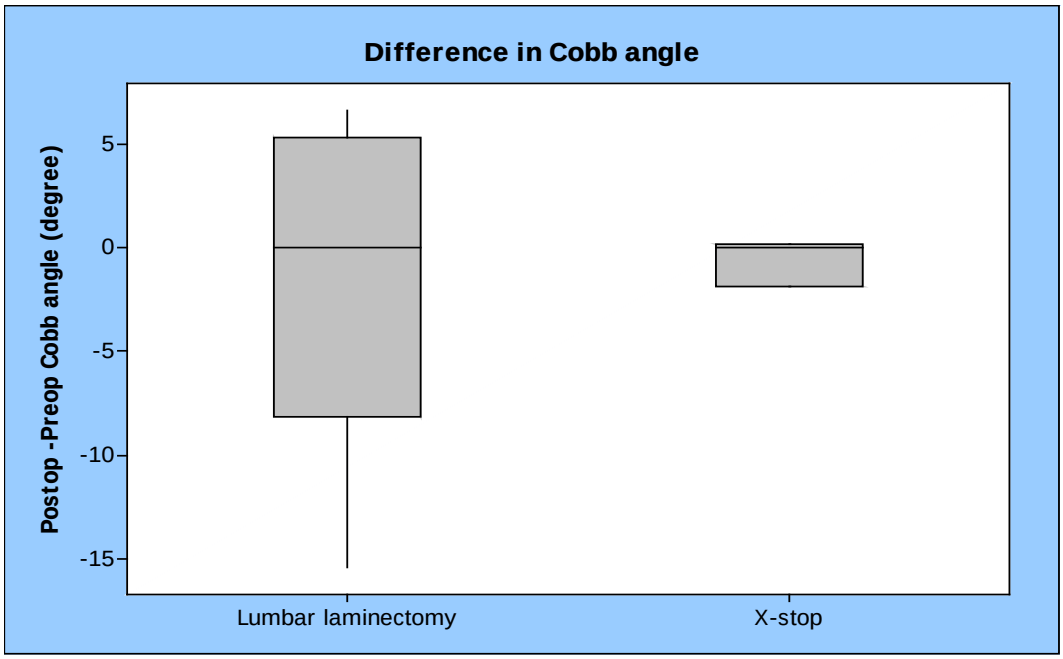


Figure 4.41: Boxplot of change of preoperative and postoperative Cobb angles for two treatment groups.

Table 4.43: Preoperative, postoperative and change in Cobb angles (degrees). IQR=Interquartile range.

	Procedure	Number of patients	Median	IQR	p-value
Preoperative	LL	5	18.2	19.2	-
	XS	3	9.9	22.3	
Postoperative	LL	5	13.5	16.9	-
	XS	3	9.9	20.2	
Change in Cobb angle	LL	5	0.0	13.4	0.881
(mm)	XS	3	0.0	2.1	

4.8.2. Adjacent Spinal Segment Changes

4.8.2.1. Upper adjacent spinal canal area

(above the operated level(s))

There was no significant difference in the change of the spinal canal area between the two treatment groups (p= 0.551) (Figure 4.42 and Table 4.44). Also, there were no significant differences between preoperative and postoperative spinal canal area in Lumbar laminectomy (p=0.403) and X-stop (p=1.0).

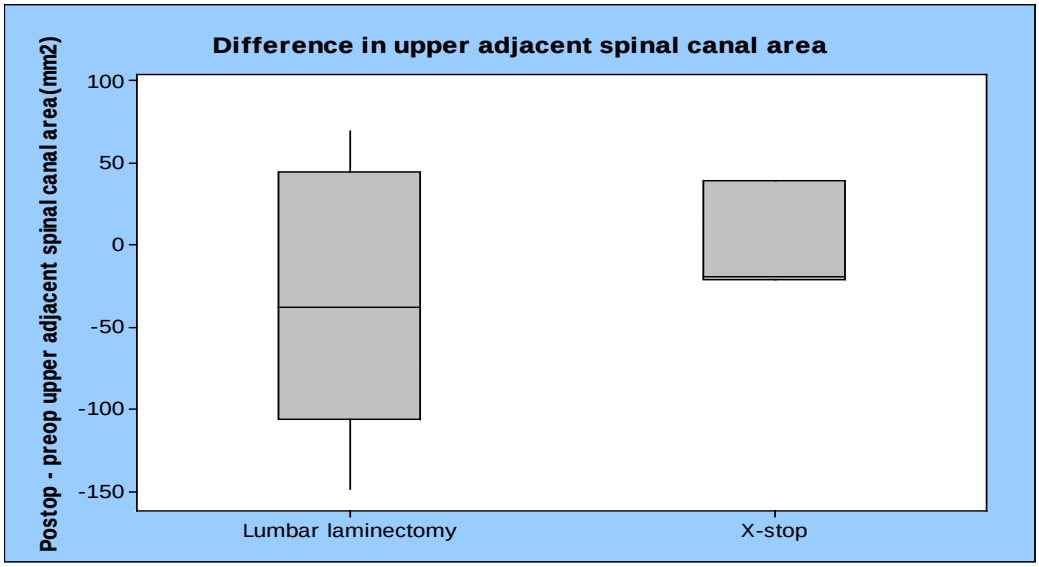


Figure 4.42: Boxplot of change of preoperative and postoperative upper adjacent spinal canal area for two treatment groups.

Table 4.44: Preoperative, postoperative and change in upper adjacent spinal canal area(mm^2) for two treatment groups. IQR=Interquartile range.

	Procedure	Number of patients	Median	IQR	p-value
Preoperative	LL	5	175.7	109.8	-
	XS	3	162.4	77.7	
Postoperative	LL	5	117.8	59.7	-
	XS	3	167.6	45.1	
Change in upper adjacent spinal canal area(mm^2)	LL	5	-37.8	150.9	0.551
	XS	3	-19.1	60.4	

4.8.2.2. **Upper adjacent intervertebral foraminal area**
(above the operated level(s))

There was no significant difference in the change of the foraminal area between the two treatment groups (p=0.136) (Figure 4.43 and Table 4.45). Also, there were no significant differences between preoperative and postoperative foraminal area in Lumbar laminectomy (p=0.676) and X-stop (p=0.662).

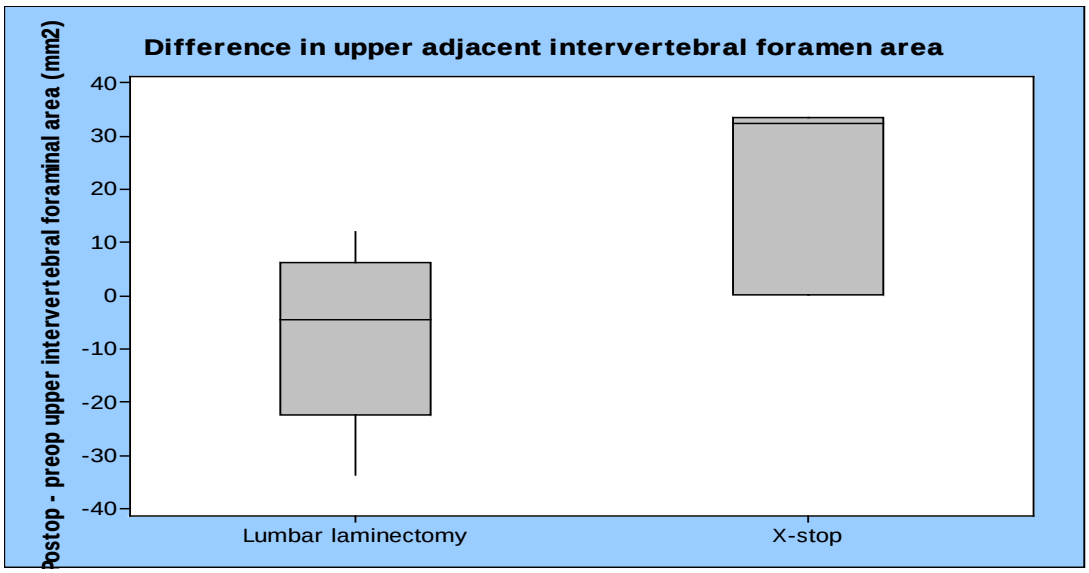


Figure 4.43: Boxplot of change of preoperative and postoperative upper adjacent intervertebral foraminal area for two treatment groups.

Table 4.45: Preoperative, postoperative and change in upper adjacent intervertebral foraminal area(mm^2) for two treatment groups. IQR=Interquartile

	Procedure	Number of patients	Median	IQR	p-value
Preoperative	LL	5	67.7	41.5	-
	XS	3	47.0	37.0	
Postoperative	LL	5	48.7	45.9	-
	XS	3	80.6	69.2	
Change in upper adjacent intervertebral foramina above (mm^2)	LL	5	-4.4	28.8	0.136
	XS	3	32.5	33.3	

4.8.2.3. **Upper adjacent facet size**

(above the operated level(s))

There was no significant difference in the change of the facet size length between the two treatment groups (p=0.551) (Figure 4.44 and Table 4.46). Also, there were no significant differences between preoperative and postoperative facet size length in Lumbar laminectomy (p=0.531) and X-stop (p=0.383).

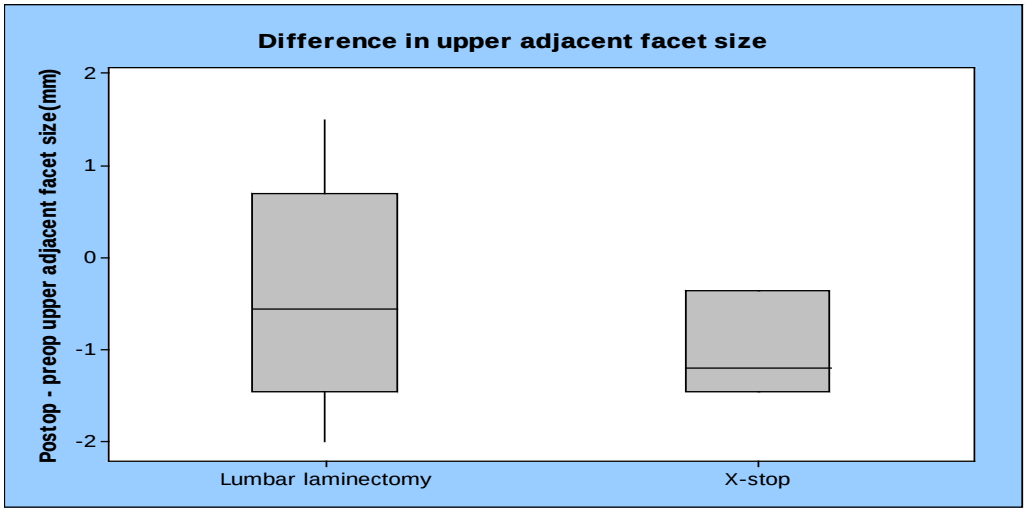


Figure 4.44: Boxplot of change of preoperative and postoperative upper adjacent facet size for two treatment groups.

Table 4.46: Preoperative, postoperative and change in upper adjacent facet size(mm) for two treatment groups. IQR=Interquartile range.

	Procedure	Number of patients	Median	IQR	p-value
Preoperative	LL	5	14.7	2.9	-
	XS	3	15.4	1.0	
Postoperative	LL	5	13.7	0.9	-
	XS	3	14.2	2.1	
Change in upper adjacent facet size length (mm)	LL	5	-0.5	2.1	0.551
	XS	3	-1.2	1.1	

4.8.2.4. **Lower adjacent spinal canal area**

(Below the operated level(s))

There was no significant difference in the change of the spinal canal area between the two treatment groups (p=1.0) (Figure 4.45 and Table 4.47). Also, there were no significant differences between preoperative and postoperative spinal canal area in Lumbar laminectomy (p=0.403) and X-stop (p=1.0).

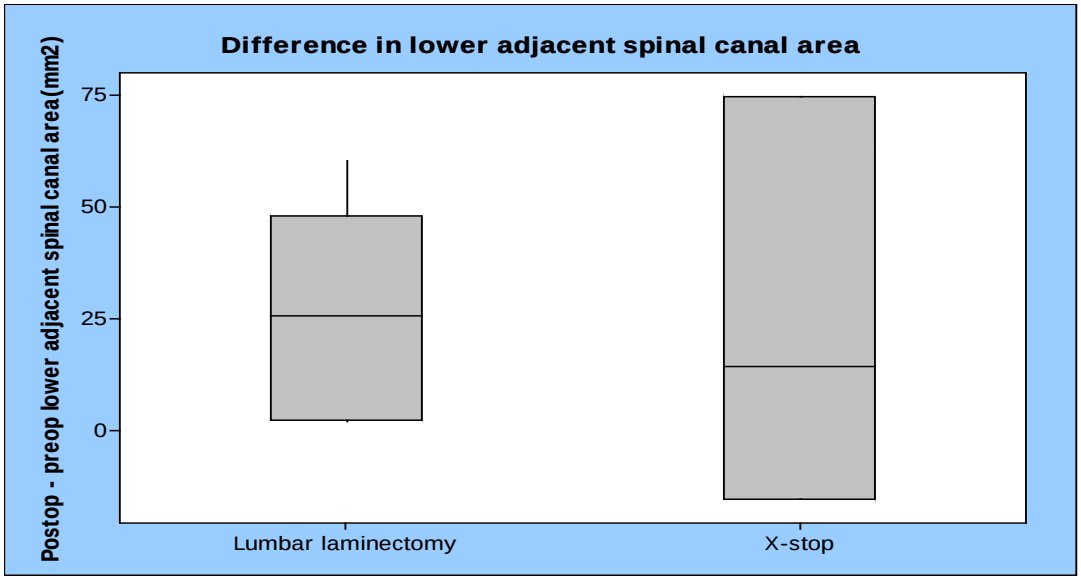


Figure 45: Boxplot of change of preoperative and postoperative lower adjacent spinal canal area for two treatment groups.

Table 4.47: Preoperative, postoperative and change in lower adjacent spinal canal area(mm^2) for two treatment groups. IQR=Interquartile range.

	Procedure	Number of patients	Median	IQR	p-value
Preoperative	LL	5	150.3	66.5	-
	XS	3	149.5	59.4	
Postoperative	LL	5	152.9	90.8	-
	XS	3	163.7	149.3	
Change in lower adjacent spinal canal area(mm^2)	LL	5	25.5	45.7	1.0
	XS	3	14.2	89.9	

4.8.2.5. **Lower adjacent intervertebral foramen area**
(below the operated level(s))

There was no significant difference in the change of the foraminal area between the two treatment groups (p=0.371) (Figure 4.46 and Table 4.48). Also, there were no significant differences between preoperative and postoperative foraminal area in Lumbar laminectomy (p=1.0) and X-stop (p=0.190).

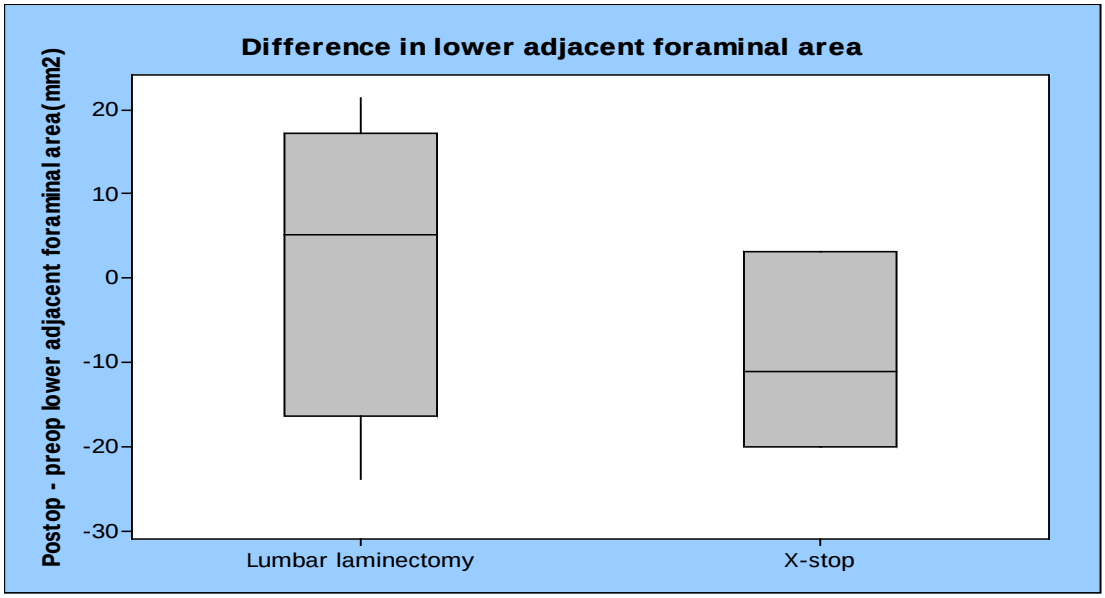


Figure 4.46: Box plot of change of preoperative and postoperative lower adjacent intervertebral foraminal area for two treatment groups.

Table 4.48: Preoperative, postoperative and change in lower adjacent intervertebral foraminal area(mm^2) for two treatment groups. IQR=Interquartile range.

	Procedure	Number of patients	Median	IQR	p-value
Preoperative	LL	5	73.3	43.1	-
	XS	3	66.0	16.8	
Postoperative	LL	5	64.5	44.8	-
	XS	3	57.6	8.9	
Change in lower adjacent intervertebral foramen area(mm^2)	LL	5	5.1	33.5	0.371
	XS	3	-11.0	23.1	

4.8.2.6. **Lower adjacent facet size**

(below the operated level(s))

There was no significant difference in the change of the facet size length between the two treatment groups (p=0.551) (Figure 4.47 and Table 4.49). Also, there were no significant differences between preoperative and postoperative facet size length in Lumbar laminectomy (p=0.754) and X-stop (p=0.383).

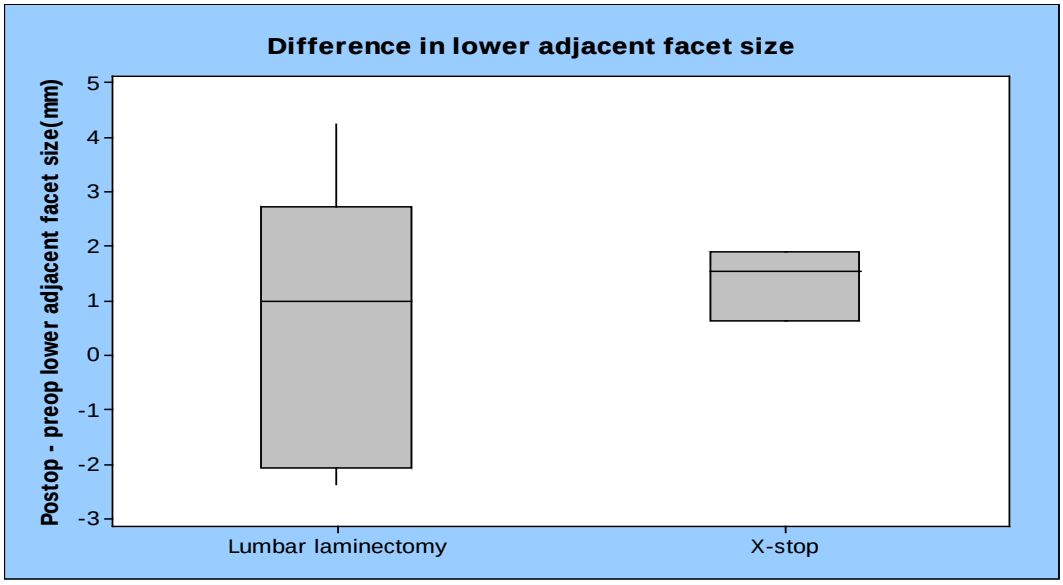


Figure 4.47: Boxplot of change of preoperative and postoperative lower adjacent facet size for two treatment groups.

Table 4.49: Preoperative, postoperative and change in lower adjacent facet size (mm) for two treatment groups. IQR=Interquartile range.

	Procedure	Number of patients	Median	IQR	p-value
Preoperative	LL	5	16.8	3.4	-
	XS	3	18.0	3.7	
Postoperative	LL	5	16.8	4.7	-
	XS	3	19.5	2.4	
Change in lower adjacent facet size length(mm)	LL	5	1.0	4.8	0.551
	XS	3	1.5	1.2	

4.8.2.7. **Upper adjacent ligamentum flavum thickness** (above the operated level(s))

There was no significant difference in the change of the ligamentum flavum thickness between the two treatment groups (p=0.551) (Figure 4.48 and Table 4.50). Also, there were no significant differences between preoperative and postoperative facet size length in Lumbar laminectomy (p=0.676) and X-stop (p=1.0).

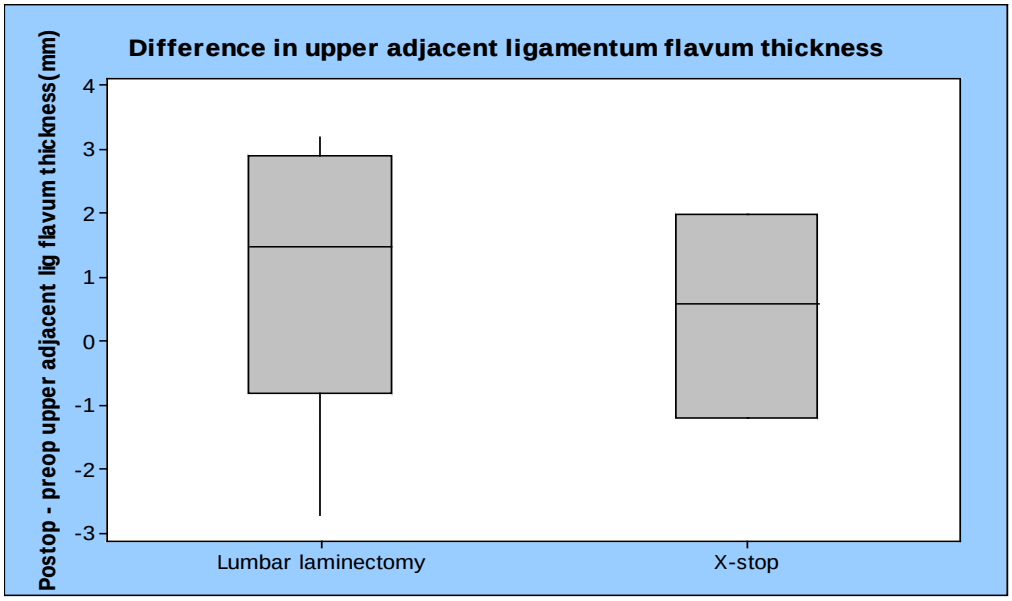


Figure 4.48: Boxplot of change of preoperative and postoperative upper adjacent ligamentum flavum thickness for two treatment groups.

Table 4.50: Preoperative, postoperative and change in upper adjacent ligamentum flavum thickness(mm) for two treatment groups. IQR=Interquartile range.

	Procedure	Number of patients	Median	IQR	p-value
Preoperative	LL	5	5.6	4.3	-
	XS	3	6.3	4.2	
Postoperative	LL	5	4.6	3.7	-
	XS	3	5.1	5.6	
Change in upper adjacent ligamentum flavum thickness(mm)	LL	5	1.5	3.7	0.551
	XS	3	0.6	3.2	

4.8.2.8. Lower adjacent ligamentum flavum thickness (above the operated level(s))

There was no significant difference in the change of the ligamentum flavum thickness between the two treatment groups (p=0.456) (Figure 4.49 and Table 4.51). Also, there were no significant differences between preoperative and postoperative facet size length in Lumbar laminectomy (p=0.917) and X-stop (p=1.0).

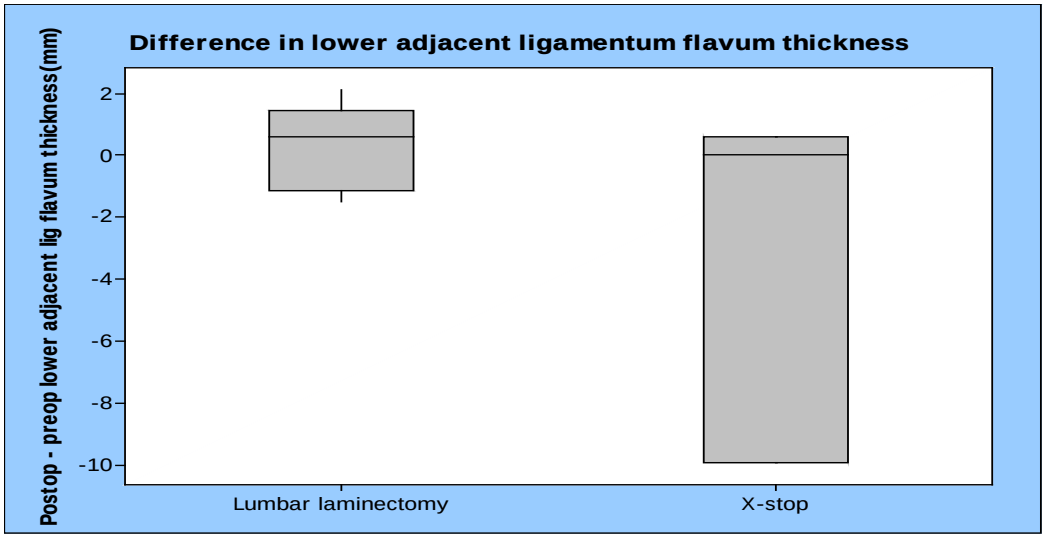


Figure 4.49: Boxplot of change of preoperative and postoperative lower adjacent ligamentum flavum thickness for two treatment groups.

Table 4.51: Preoperative, postoperative and change in lower adjacent ligamentum flavum thickness(mm) for two treatment groups. IQR=Interquartile range.

	Procedure	Number of patients	Median	IQR	p-value
Preoperative	LL	5	4.3	1.3	-
	XS	3	4.1	10.5	
Postoperative	LL	5	3.9	3.0	-
	XS	3	4.1	0.0	
Change in lower adjacent ligamentum flavum thickness(mm)	LL	5	0.6	2.6	0.456
	XS	3	0.0	10.5	

4.8.2.9. Upper adjacent disc height

(above the operated level(s))

We found that there was a significant loss of disc height in the upper adjacent spinal (i.e. above the operated level(s)) in Lumbar laminectomy group compared to X-stop group (p=0.0369). This suggests accelerated degenerative changes in Lumbar laminectomy group compared to the X-stop group (Figure 4.50 and Table 4.52). However, there were no significant differences between preoperative and postoperative disc height in Lumbar laminectomy (p=0.754) and X-stop (p=0.383) separately.

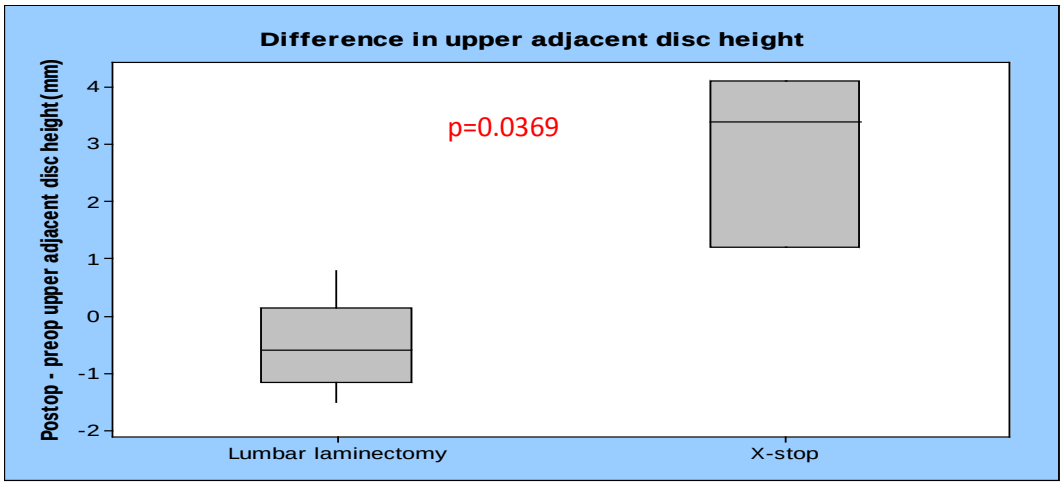


Figure 4.50: Boxplot of change of preoperative and postoperative upper adjacent disc height for two treatment groups.

Table 4.52: Preoperative, postoperative and change in upper adjacent disc height(mm) for two treatment groups. IQR=Interquartile range.

	Procedure	Number of patients	Median	IQR	p-value
Preoperative	LL	5	9.4	2.9	-
	XS	3	7.6	5.2	
Postoperative	LL	5	8.9	4.0	-
	XS	3	11.7	7.4	
Change in upper disc height(mm)	LL	5	-0.6	1.3	0.0369
	XS	3	3.4	2.9	

4.8.2.10. **Lower adjacent disc height**

(above the operated level(s))

There was no significant difference in the change of the lower adjacent disc height between the two treatment groups (p=0.136) (Figure 4.51 and Table 4.53). Also, there were no significant differences between preoperative and postoperative lower adjacent disc height in Lumbar laminectomy (p=1.0) and X-stop (p=0.662).

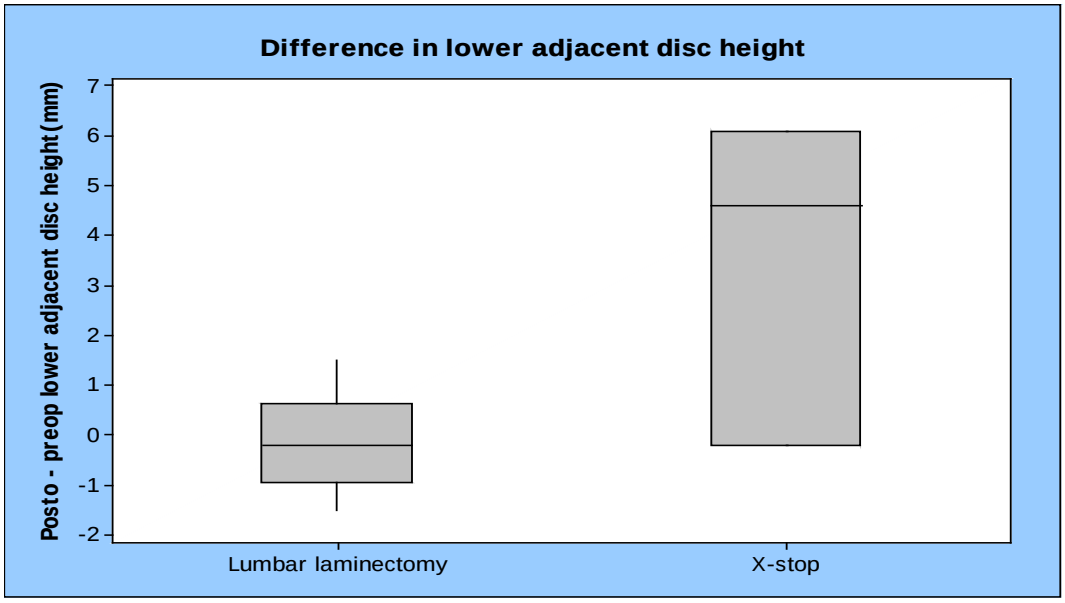


Figure 4.51: Boxplot of change of preoperative and postoperative lower adjacent disc height for two treatment groups.

Table 4.53: Preoperative, postoperative and change in lower adjacent disc height(mm) for two treatment groups. IQR=Interquartile range

	Procedure	Number of patients	Median	IQR	p-value
Preoperative	LL	5	11.3	4.2	-
	XS	3	6.0	2.4	
Postoperative	LL	5	11.6	5.4	-
	XS	3	12.1	7.2	
Change in lower adjacent disc height(mm)	LL	5	-0.2	1.6	0.136
	XS	3	4.6	6.3	

4.9. **COMPLICATIONS**

In our study, 6 out of 10 (60%) patients crossed from the X-stop group to the Lumbar laminectomy following the X-stop insertion. This makes it a rather high reoperation rate in the X-stop group. 1 out of 6 patients who was reoperated, had spinous process fracture while the others showed either no improvement or worsening of symptoms. Hence removal of X-stop and revision operation with Lumbar laminectomy was performed.

Table 4.54: Number of patients who were reoperated. Note: The only reoperation was removal of X-stop device and lumbar laminectomy.

	Number of patients reoperated (Percentages)		
	No	Yes	Total
Procedure			
LL	10(100)	0(0)	10
XS	4(40)	6(60)	10

4.10. **FOLLOW UP**

We have had no loss to follow up. All patients were followed up to 12 months postoperatively.

4.11. SAMPLE SIZE CALCULATION

We have used our pilot study data to guide the sample size in continuation of the study (Table 4.55).

With Significance level 0.05, with Power 0.80 we calculated that we need total of:

- 50 participants to detect a significant effect size 10% (less than 2.50 score) for ZCQ Satisfaction component (25 in each group)
- 28 participants to detect a significant effect size 10% (0.5 score) for ZCQ Symptom component (14 in each group) or
- 14 participants to detect a significant effect size 12.5% (0.5 score) for ZCQ Physical component (7 in each group).

It is suggested that using the larger estimated sample size of 50 participants for ZCQ Satisfaction component should suffice for ZCQ Symptom and Physical component, which both require smaller sample size (Table 54).

Table 4.55: Sample size calculated values to achieve a significant size effect of 10% (0.5) in ZCQ Symptom, 12.5% (0.5) Physical component and 12.5%(2.5) Satisfaction component at 12 months, with significance level 0.05, power 0.80.

	Procedure	Mean(%)	StDev	StDev pooled	Sample size required
ZCQ Symptom preoperative	LL	72.14	16.82	14.76	28(14 in each group)
	XS	71.43	12.37		
ZCQ Physical preoperative	LL	66.88	13.19	12.98	14(7 in each group)
	XS	63.75	12.77		
ZCQ Satisfaction Scale at 12 months	LL	56.67	23.99	24.75	50(25 in each group)
	XS	52.08	25.48		

Reason for the stated size effects:

As previously suggested (128), the criteria of success of operations in LSS are the difference of greater than 0.5 in ZCQ Symptom and Physical component as well as mean score of less than 2.50 in Satisfaction component.

The required percentage difference effects that we have used in power calculations come from the fact that:

- Difference in ZCQ Symptom component greater than 0.5 is considered as significant. Now, as ZCQ Symptom component scores from 1- 5 the conversion between the percentage and score is:

  ZCQ Symptom component score =(ZCQ Symptom component percentage x5)/100.

  Since the required score difference is 0.5, this converts to Percentage as follows:

  Percentage of 0.5 score = 0.5 x 20 = 10% is the required percentage difference effect.

- Similarly, the required difference effect for ZCQ Physical component (which scores 1 – 4) is 0.5 and is converted to percentage as follows:

  ZCQ Physical component score =(ZCQ Physical component percentage x4)/100.

  Since the required score difference is 0.5, this converts to Percentage as follows:

  Percentage of 0.5 score = 0.5 x 25 = 12.5% is the required percentage difference effect.

- The required difference effect for ZCQ Satisfaction component is to get score difference of 2.50 which is**:**

  ZCQ Satisfaction component score =(ZCQ Satisfaction component percentage x4)/100.

  Therefore,

  Percentage of 2.50 score = 2.5 x 25 = 12.5% is the required percentage difference effect of ZCQ Satisfaction component.

4.12. CORRELATION BETWEEN GENERAL QUALITY OF LIFE AND DISEASE-SPECIFIC OUTCOME MEASURES

Convergent validity was assessed by computing correlations between the specific and generic outcome scores.

Convergent validity was shown by strong correlations between disease-specific scores and quality of life as follows:

- There is a strong correlation between ZCQ Physical component and EQ5D score and
- There is a strong correlation between ZCQ Symptom component and SF36 domains: Bodily pain.
- There is a strong correlation between ZCQ Physical component and SF36 domains:

Physical functioning, Bodily pain, General Health, Vitality and Social functioning.

Table 4.56: Correlation between quality of life questionnaires (EQ5D and SF36 domains) and Zurich claudication questionnaires. Pearson correlation coefficient (r) used. RED indicates significant results.

	p-value			
	Zurich claudication questionnaire			
	Symptom component		Physical component	
Variables	**r**	**p-value**	**r**	**p-value**
EQ5D	-0.284	0.225	-0.551	0.012
SF36				
PF	-0.441	0.052	-0.629	0.003
RP	0.283	0.227	-0.027	0.910
BP	-0.709	<0.001	-0.530	0.016
GH	-0.388	0.091	-0.564	0.010
VT	-0.320	0.170	-0.484	0.031
SF	-0.273	0.245	-0.511	0.021
RE	0.231	0.326	-0.048	0.842
MH	-0.125	0.599	-0.352	0.128

Table 4.57: Correlation between quality of life questionnaires (EQ5D and SF36 domains) and disease-specific questionnaires (Oswestry Disability Index score, Quebeck Back Pain Disability Scale). Pearson correlation coefficient (r) used. RED indicates significant results.

Disease-specific questionnaires				
	ODI		**QBPDS**	
Variables	**r**	**p-value**	**r**	**p-value**
EQ5D	-0.394	0.086	-0.285	0.223
SF36				
PF	-0.533	0.015	-0.749	<0.001
RP	0.005	0.983	0.218	0.355
BP	-0.623	0.003	-0.629	0.003
GH	-0.497	0.026	-0.475	0.034
VT	-0.485	0.030	-0.520	0.019
SF	-0.361	0.118	-0.512	0.021
RE	-0.269	0.251	-0.096	0.688
MH	-0.244	0.300	-0.423	0.063

4.13. **SUMMARY OF FINDINGS**

Quality of life

- There was no difference in EQ5D dimensions and SF36 domains between the two treatment groups.
- No improvements were detected between the two treatments but there is evidence to suggest improvements in quality of life within each treatment group over time.

QALYs

- There were no significant differences in QALYs gained for either intervention

Costs

- The costs were significantly higher for the X-stop group. This seems to be related to the cost of the implant because no significant differences were found between costs associated with theatre time, inhospital stay, physiotherapy sessions and neurosurgery outpatient attendances.

Cost-effectiveness

- The base case estimates have shown that incremental cost effectiveness ratio (ICER) is dominant suggesting that Lumbar laminectomy is a better value for money but with small probability suggesting the need for a larger trial.

Clinical outcomes

- No improvements in back pain outcomes were found using QBPDS and ODI.
- However, there were significant improvements in ZCQ Symptom component and Physical components for each intervention separately but

not when compared with each other. This improvement is noted from 6 weeks and remains until 12 months period for both interventions.

Predictive factors

- **ASA score –** is a NEGATIVE predictive factor for Cost and ZCQ Symptom component, and POSITIVE predictive factor for ZCQ Physical component.

- **Actual level operated –**the lower the level operated (e.g. L4/5 compared to L3/4) a NEGATIVE predictive factor for GH, RE, RP, and POSITIVE predictive factor for ZCQ Physical component.

- **Age** – is a POSITIVE predictive factor for the Cost.

- **BMI –**is a NEGATIVE predictive factor for Cost and ZCQ Physical component.

- **Duration of symptoms –** is a NEGATIVE predictive factor for Cost.

- **Levels (number of levels operated) –** is a NEGATIVE predictive factor for EQ5D score

- **Smoking –** is a NEGATIVE predictive factor for Mental Health.

- **VAS pain score –** is a NEGATIVE predictive factor for Cost, and POSITIVE predictive factor for BP and SF.

Other factors such as Gender, Procedure (X-stop or Lumbar laminectomy) and Cobb angle did not have a significant predictive value on the outcome measures in multivariate regression analysis.

Correlation between general quality of life and disease-specific questionnaires

- There is significant evidence to suggest convergent validity of EQ5D score and SF36 with ZCQ Symptom and Physical component because of their significant correlation. This proves the validity of using the EQ5D and SF36 domains in patients with lumbar spinal stenosis.
- There is significant evidence to suggest convergent validity of SF36 with Oswestry Disability Index and Quebeck Back Pain Disability scale. This proves the validity of using the SF36 domains is appropriate to use in relationship to lower back pains in patients with lumbar spinal stenosis.

Radiological changes associated with each intervention.

- *Operative level:-* No difference was found between two treatment groups in postoperative changes in spinal canal area, intervertebral foraminal area, anterior disc height, posterior disc height, facet size, intervertebral angle, Cobb angle.

- *Adjacent levels* – It was found that the Lumbar laminectomy causes a significantly greater loss of upper disc height compared to the X-stop group ($p= 0.037$) which could represent an evidence of greater upper vertebral degeneration in Lumbar laminectomy group or simply biomechanical widening of upper disc height secondary to the upward stress force applied by the X-stop device to the vertebra above. No difference was found between two treatment groups in postoperative changes in upper and lower adjacent spinal canal area, intervertebral foraminal area, facet size and ligamentum flavum thickness.

Complications:

- Six out of ten patients in XS group had X-stop removed and laminectomy performed over the affected stenosed levels. This constitutes a 60% revision rate for the XS group in our study.

Sample size calculations

- From our current results of the pilot study, a future randomised study should be powered to recruit 50 participants in each group i.e. 25 participants in each group (Power 80%, p=0.05).

5. DISCUSSION

The work for this thesis is generated by a high quality randomised controlled trial having as a primary end-point to compare which one, lumbar laminectomy or X-stop procedures is more cost-effective.

5.1. Demographic data

The baseline demographics data are comparable (Table 4.2 and 4.3) between the two treatment groups.

5.2. Quality of life

It was shown that the EQ-5D is useful tool for estimating health state values and for monitoring outcome of patients undergoing low-back surgery. Hence, this instrument is useful in providing valid data for cost– utility analyses in lower back surgery.(135)

The assessment of quality of life between lumbar laminectomy and X-stop in lumbar spinal stenosis has not been previously done by using the EQ5D instrument. One study have shown that there was an improvement in EQ5D postoperatively following lumbar laminectomy operation.(136)

This is in keeping with our findings of improvement of quality of life in Lumbar laminectomy group. Improving trends in quality of life were also noted within the X-stop group in our study but this failed to reach significance due to small sample size.

In order to capture further quality of life data we have also used SF36 instrument. It has been suggested that SF-36 domain scores are valid for measuring morbidity and surgical outcomes in common spinal disorders including lumbar spinal stenosis patients.(134) A randomised controlled trial showed an improvement in quality of life by using SF36 domains in the X-stop group compared to conservative treatment group at 6-week, 6-month, and 1-year post-treatment follow-up time points.(128) In the same study, the X-stop group scored significantly better than the conservative group in every domain. In addition,it was found that even within the X-stop group alone there were significant

postoperative improvements in the mean scores in each category than the respective preoperative scores. Same study found no significant improvement in the conservative group.(128)

Another study showed that mean General Health (GH), Role Emotional, and Mental Component scores continued improving at 2 years in the X-stop group.(150)

Similarly, a long-term follow-up study showed that patients operated on for lumbar stenosis continue to improve their quality of life pattern even between the 4th and the 8th year after surgery. Specific improvements were observed in Physical Function, Bodily Pain, Mental Health and the Physical Function scores with respect to the first follow- up. However, Vitality worsened during this follow up.(137)

But how does quality of life compares between lumbar laminectomy and X-stop treated patients for LSS?

To our knowledge, no previous studies have directly compared Lumbar laminectomy and X-stop in a randomised fashion. One study previously has pooled results from various studies and found no difference in quality of life between X-stop and Lumbar laminectomy over 2-year period.(163) We also found that there was no difference between the two treatment groups in all domains of SF36 within 1-year. When assessed separately the X-stop group showed significant improvements in Physical functioning at 6 weeks and Bodily pain at 12 months. Lumbar laminectomy group alone showed an improvement only in Bodily pain at 6 weeks. It may be that the differences in quality of life between the two treatment groups may appear after a follow up longer than 1 year so a longer and larger sample size is required.

5.3. Cost-effectiveness

No differences in utility values (QALYs) were found between the two treatment groups. However, the costs were significantly higher in the X-stop group. This seems to be related to the cost of the implant because no significant differences were found for costs associated with time in theatre, inhospital stay, physiotherapy sessions and neurosurgery outpatient attendances between the two treatment groups.

In order to increase external validity and make the results more generalisable the operations were performed as per routine NHS lists. That is, either consultants or their senior neurosurgical registrars performed the XS or LL. Perhaps if only consultants performed both procedures then the timing of surgery would be shorter and costs may be saved. However this shortening of intraoperative time would apply to both procedures.

Similarly previous studies found no significant difference in QALYs between X-stop and Lumbar laminectomy when data were pooled from literature search.(163) However, this study found that there was a lower cost associated with X-stop treatment compared to lumbar laminectomy.

There is a study supporting the use of the X-stop over lumbar laminectomy on the grounds of higher cost-effectiveness. In this study, patients were randomly allocated to X-stop and conservative treatment. Cost data from patients who failed conservative treatment and went into lumbar laminectomy were used, the process that would have introduced selection bias as a result of choosing a poorer performing cohort of one of the treatment arms.(141)

We differ in our results where we found that the costs were significantly lower in Lumbar laminectomy group. The results of costs and QALYs led to calculating a dominant base-case estimate, that is, incremental cost effectiveness ratio suggesting that Lumbar laminectomy is *dominant* i.e. 'better value for money' compared to the X-stop intervention.

The uncertainty regarding the maximum acceptability values showed that for the suggested NHS ceiling of about £30000 per QALY there is a 0.544(for EQ5D-derived utilities) and 0.512(for SF36-derived utilities) probability that Lumbar laminectomy is more cost-effective than X-stop. This finding somehow weakens the statement of dominance of lumbar laminectomy when current threshold value is suggested. This suggests that there are strong grounds to continue with current study to increase the number of participants and re-analyse the cost data.

5.4. Clinical outcomes

There are a number of disease-specific questionnaires utilised in assessment of spinal disorders. By using more than one questionnaire for QoL and clinical

outcomes, we have attempted to capture as much subtle variations between the two treatment groups.

There is evidence to suggest that both X-stop and Lumbar laminectomy procedures are superior to conservative treatments.

The RCTs such as The Finnish Lumbar Spinal Research Group (94) and The SPORT study(98) showed that lumbar laminectomy was superior to conservative treatment in patients with lumbar spinal stenosis.

Our data suggest that QBPDS and ODI did not show any improvement between- and within-treatment groups, while significant improvements were observed in ZCQ Symptom and Physical component when mean preoperative and postoperative scores were assessed within each treatment group. These improvements remain until 12 weeks postoperatively for each treatment group separately. Our finding regarding the X-stop group alone, are in keeping with previous study where improvements in X-stop group compared to conservative treatment were significant.(128) We found no improvements in clinical outcomes between and within treatment groups over 1-year when QBPDS and ODI instruments were used. Previous RCT study found a significant improvement in X-stop group compared to conservative treatment over 2 years.(131) Same study, at 4-year follow-up, showed an improvement in clinical outcome (132) where ODI was used as an outcome instrument. Limitations of this study are a high rate of loss to follow up ending up with a small sample size and no indication that statistical testing was performed. Also, no control group was present in the 4-year follow up.

A prospective observational study was performed to assess the clinical outcome of patients with symptomatic lumbar spinal stenosis before and at periodic intervals after the X-stop was implanted. Forty consecutive patients were enrolled and surgically treated with this device, which was implanted at the level of stenosis, either at 1 or 2 levels in each patient. Patients were clinically evaluated at the preoperative, 3-month, 6-month, and 1-year stage with questionnaires (Zurich Claudication Questionnaire, Oswestry Disability Index, and SF-36). By 12 months, over half (54%) of the patients with implanted X-stop devices reported clinically significant improvement in their symptoms, 33% reported clinically significant improvement in ZCQ Physical function, and 71% expressed

satisfaction with the procedure. The mean ODI score showed maximal improvement at the 3-month visit (preoperative: 48%; range, 24%– 62%; 3 months: 35%; range, 4%–64%) with very little change subsequently.
Regarding quality of life, the mean Physical function, Bodily pain, and Physical cumulative scores of the SF-36 showed maximal increase in the first 3 months after surgery. The Role physical score continued to improve up to the 1-year postoperatively.(133) Limitations of this study were small sample size, high rate of loss to follow up and no p-values or confidence intervals of the outcome measures given to indicate the strength of evidence.
The success rates in our study showed an apparent 60% success rate of the X-stop group at 12 months period. However this should take into consideration that this was an intention-to-treat analysis with a 60% cross-over from the X-stop to lumbar laminectomy group.

5.5. Predictive factors

Studies of factors associated with outcome generally have been small, retrospective, and limited in the number and types of potential predictor variables analyzed.(113)
A systematic review has shown that depression, cardiovascular comorbidity, disorder influencing walking ability, and scoliosis predicted poorer subjective outcome. Better walking ability, self-rated health, higher income, less overall comorbidity, and pronounced central stenosis predicted better subjective outcome. Male gender and younger age predicted were associated with better postoperative walking ability. The predictive value may be outcome specific, therefore the use of all relevant outcome measures is recommended when studying predictors of LSS.(164)
On the contrary to this systematic review, we found no predictive value with gender or degree of scoliosis, for any of quality of life or disease specific outcomes. However, in our study, younger age was associated with lower costs regardless of which intervention was performed.
Another study suggests that longer duration of symptoms (over 33 months) is associated with functional outcome (as measured by the ODI). Limitations are that the predictor effect of duration of symptoms was only noted in subgroup

analysis.(165) In our study, multivariate analysis showed that preoperative duration of symptoms was negatively associated with costs. That is, the longer the duration of symptoms preoperatively was associated with lower the costs over 1 year, and did not show significant predictive value for other outcome measures. It is difficult to explain why longer duration of symptoms preoperatively may lead to lower costs. This negative relationship between duration of symptoms and cost persisted even when we excluded one patient with shorter duration of symptoms whose X-stop was removed and had persistence of symptoms requiring additional imaging, physiotherapy sessions and hence much larger costs compared to other participants. This unexpected result may be a due to small sample size.
A better understanding of prognostic factors could enable patients and surgeons to develop better expectations concerning the operative outcomes.

5.6. Correlation between general quality of life and disease-specific questionnaires

Predictive validity of general quality of life questionnaires can be demonstrated by correlations between pre- and post-operative scores for specific and generic instruments. One study found that Physical Function, Bodily Pain, and Mental Health domains were all significantly correlated with clinical responsiveness such as VAS pain score. This suggested that SF-36 domain scores is considered valid for measuring morbidity and surgical outcomes in common spinal disorders.(134) In our study, we found that there is significant evidence to suggest convergent validity of EQ5D score and SF36 with ZCQ Symptom and Physical component because of their significant correlation. We also found significant evidence to suggest convergent validity of SF36 with Oswestry Disability Index and Quebeck Back Pain Disability scale. These findings prove the validity of using the EQ5D score and SF36 domains appropriate to use in relationship to lower back pains in patients with lumbar spinal stenosis.

5.7. Radiological changes associated with each intervention

It has been shown that degenerative changes in the lumbar spine are very common in the asymptomatic population, especially in patients over 60 years of age, 20% will reveal signs of LSS.(64)

Therefore, only the clinical correlation to radiological findings is important to be evaluated.

Previous studies have shown that after implantation of the interspinous device there was a significant increase ($P<0.0001$) of the foraminal height, foraminal width, foraminal cross-sectional area, intervertebral angle and decrease in anterior disc height and posterior disc height.(138)
Another study showed that in 12 patients with 17 distracted levels, the area of the dural sac at these levels increased from 77.8 to 93.4 mm^2 after surgery in the standing position ($P = 0.006$), with increase in the exit foramens, but no change in lumbar posture. This study shows that the X-stop device increases the cross-sectional area of the dural sac and exit foramens without changes in posture.(139)

In our study, no difference was found between two treatment groups in postoperative changes in spinal canal area, intervertebral foraminal area, anterior disc height, posterior disc height, facet size, intervertebral angle and Cobb angle at the operated level.
However, we found that the Lumbar laminectomy causes a significantly greater loss of upper disc height compared to the X-stop group ($p= 0.037$) as an evidence of greater upper vertebral degeneration in Lumbar laminectomy group or simply biomechanical widening of upper disc height secondary to the upward stress force applied by the X-stop device to the vertebra above. Also our results suggests that there is a decrease in lower adjacent intervertebral foramen area following the X-stop insertion in the XS group only (Table 4.48). However, this result was insignificant which could be due to a too small sample size.
No difference was found between two treatment groups in postoperative changes in upper and lower adjacent spinal canal area, intervertebral foraminal area, facet size and ligamentum flavum thickness.

5.8. *Complications*

Turner et al in 1992 showed the following complication rates for lumbar decompressive surgery: perioperative mortality (0.32%), dural tears (5.91%), deep infection (1.08%), superficial infection (2.3%) and DVT (2.78%).(106)

On the other side, the reported complications of the X-stop are: malpositioned implant(1%), implant dislodgement/migration (1%), spinous process fracture (1%) and increased pain at implant level (1%). (131)
Another study reported 5.7% device dislodgment and 5.7% of spinous process fractures.(166) In our study we had two dural tears in Lumbar laminectomy group and two spinous process fractures in the X-stop groups. This makes for the complication rates of 20% in both treatment groups.

5.9. *Reoperation*

In our study, there were 60% revision operations of removal of X-stop with concomitant lumbar laminectomy. No lumbar laminectomy patients were reoperated. The reported reoperation rate in another RCT for the X-stop patients was 6%.(131)

5.10. *Sample size calculations*

Initial sample size calculation was done based on the data from another study (149) and found that we needed 55 patients in each group, taking into consideration the losses to follow up in that study. In Katz study the required effect difference in cost was chosen at 20% and the loss to follow up was 27%. Prior to commencement of our study, Katz study was the only one with available cost parameters that we could use for the purpose of power calculation. The limitation of Katz study was that evaluation of costs were made between Lumbar laminectomy with and without arthrodesis where no X-stop device was used. Therefore the sample size calculation was only used as a crude guide to estimate the sample size required for our study. The limitation of initial power calculation was ameliorated using our original data from our pilot study to calculate a more appropriate sample size.Other recruitment problems that we encountered included difficulty to find patients who fulfil all eligibility criteria, and some patients decided not to opt for the operation None of the eligible patients preferred one surgical treatment over the other one.

Our study suggests that there may be some difference in cost with lumbar laminectomy being perhaps cheaper than X-stop. However, in our study, no between group differences were found with respect to clinical outcomes, which is

likely to be due to small sample size. For the cost-effectiveness study to be valid, it is required that the study is powered to detect clinical outcome differences between the two procedures too. The success of clinical outcome in lumbar spinal stenosis patients, as previously mentioned, is based on criteria of improvement in mean ZCQ Symptom and Physical component scores greater that 0.5 and ZCQ Satisfaction score less than 2.5.(128) Using our original data we found that in order to detect the required differences in clinical outcomes, our study should be powered to recruit 50 participants in each group i.e. 25 participants in each group.

6. LIMITATIONS OF THE STUDY

This study analysis is made from a small number of participants. Hence, the data is useful as it constitutes the framework for further research.

Blinding

The study is not blinded and due to nature of the interventions, this would be difficult to achieve, because both patients and surgeons often wish to know which procedure has been performed. This means that potentially observer bias may have been introduced.

Cross-over

Large cross-over from the X-stop group into the Lumbar laminectomy (60%) makes the intention-to-treat analysis cumbersome. This large cross-over suggests further that either X-stop device is not as effective as previously thought or this result was obtained as surgeons of various operative skills operated on different patients, introducing some heterogeneity in success rate. The small sample size in our study does not allow us to come to firm conclusions, but that a larger study is required. In the 6 patients who crossed over, the quality of life measures improved after laminectomy in 2 patients.

Use of statistical tests

The consequence of our small sample size is the higher likelihood of generating false negative results when statistical tests are used. For example, preoperative mean spinal canal area in LL group was almost double compared to that of the XS group (89.7% vs 54.8%, LL vs XS respectively). Also, preoperative mean Cobb

angle was over twice greater than the XS group (12.6^0 vs 5.6^0, LL vs XS respectively). However, in both cases no statistical significance was found.

Multiple comparisons

A number of statistical comparisons were made of different parameters between the LL and XS groups, and between preoperative time period in one side and postoperatively at 6 weeks, 6 months and 12 months. Application of Bonferroni correction could have been applied for multiple comparisons which would have reduced some of the significance results found.

Outcome measures

The study could have been improved by using more objective neurological scales such as: scales available to assess the gait speed (e.g., time walked test), sensory function (e.g. vibration sensation threshold), weakness (e.g. MRC power scale, maximal hip flexion using a dynamometer) or sphincter function.

Previous studies have shown an increase latency of tibial F-wave in LSS patients when electromyography studies are used (83)(84). EMG studies could be used in future studies to distinguish patients that will do better with LL or XS. However the limitation of EMG would arise in patients with concomitant diseases predisposing to polyneuropathy e.g. diabetes.

The need for additional lateral radiographs in flexion and extension to rule out segmental instability is not routinely required, as segmental instability can be detected on routine lateral radiographs in a reasonably accurate manner.(62)(71) It is shown that no additional benefits were conferred from these additional views (62)(70). However those studies were not done for the purpose of comparing XS versus LL patients. Therefore various radiological parameters (e.g. interspinous process distance changes) can be measured in flexion-extension views and the predictive effects analysed. So dynamic flexion-extension plain X-rays of lumbar region done preoperatively could prove useful as predictors of which patients will do better with which surgical procedure i.e. XS or LL.

Success rate

As discussed earlier the success rates may be related to the fact that more than half of the cases had LL after the X-stop procedure.
No intra-observer reproducibility was calculated for this study which we shall perform in a bigger study.

More centres could be included to increase the external validity of the study and reduce the time to finish the study.
ASA score has been used as a co-morbid level but we could have improved the study by using more sophisticated instruments such as Cumulative Illness Rating Scale.(168)

7. CONCLUSION

Finally, our study showed that there is some evidence that lumbar laminectomy is more cost-effective than X-stop although this is a only a preliminary study with a 1-year follow-up. We found evidence that there are within-group but not between-group improvements in outcome between lumbar laminectomy and X-stop groups. The lack of finding between-group differences may be attributed to small sample size. We suggest a formal trial with 25 patients in each group to conclusively determine which treatment is better and more cost-effective.

8. CONFLICT OF INTERESTS

The sponsor for the study was the University College Hospitals NHS Foundation Trust and partial funding was provided by Medtronic Ltd. The sponsor and the funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The research fellow and the Chief Investigator had full access to all the data in the study and had final responsibility for the analysis of the data.

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10.APPENDICES

10.2. Consent form

Centre Number: ***Version 1.1***

06/03/2008

Study Number: ***08/H0711/12***

Patient Identification Number for this trial:

10.1.**CONSENT FORM**

Cost Effectiveness & Quality of Life after Treatment of Lumbar Spinal Stenosis with the XSTOP$^{PK®}$ IPD Device or Laminectomy: A Prospective Randomised trial

(Protocol Number – 07/X01)

Name of the Investigator: **Please initial box**

1. I confirm that I have read and understand the patient information sheet dated *05/03/2008 (version 1.3)* for the above study and have had the opportunity to ask questions.

2. I confirm that I had sufficient time to consider whether I want to be included in the study.

3. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

4. I understand that sections of any of my medical notes may be looked at by responsible individuals from UCLH, Kyphon Europe or from regulatory authorities where it is relevant to my taking part in research.
   I give permission for these individuals to have access to my records.

5. I agree to take part in the above study

_____	_____	_____
Name of Patient	Date	Signature
_____	_____	_____
Name of Person taking consent (if different from researcher)	Date	Signature

_____	_____	_____
Researcher	Date	Signature

(to be contacted if there are any problems)

Comments or concerns during the study:

If you have any comments or concerns you may discuss these with the Investigator / Researcher. If you wish to go further and complain about any aspect of the way you have been approached or treated during the course of the study, you should write or get in touch with the Complaints Manager, UCL Hospitals. Please quote the UCLH project number at the top this consent form.

When completed, 1 form for the patient; 1 to be kept as part of the study documentation for the trial master/investigator site file; 1 original to be kept with the hospital medical notes.

10.3..*Patient Information Sheet*

Version: 1.3

Date: ***02/05/2008***

Project ID: ***08/H0711/12***

1. <u>Study title</u>

Cost Effectiveness & Quality of Life after Treatment of Lumbar Spinal Stenosis with the XSTOP$^{PK®}$ IPD Device or Laminectomy: A Prospective Randomised trial

2. <u>Invitation paragraph</u>

You are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

3. <u>What is the purpose of the study?</u>

One of the main causes of lower back pain is due to age-related changes in the joints and ligaments of the back causing narrowing of the spinal canal where all the nerves travel, and compression of nerve roots. This condition is called Lumbar Spinal Stenosis (where “Lumbar” means lower back and “Stenosis” means narrowing). This results in a debilitating pain or heaviness in the legs that is aggravated by walking, thereby limiting mobility. Both the conventional operation of lumbar laminectomy and the use of the newer XSTOP-device are been shown to be effective methods for treatment. However little is known regarding the costs and how patients function in every day activities after they underwent one of these 2 procedures.

The purpose of this study is to document the total costs for the operative procedures, the degree of back-pain after the operations, the length of hospital stay and complication rate on short and long term basis, after having undergone either a lumbar laminectomy or the implantation of the XSTOP device. Also the quality of life before and after the 2 procedures will be evaluated by completing specific questionnaires.

The data collected from your X-rays and the study forms completed by your surgeon's staff will be analyzed to determine if there is a significant difference between these two treatments.

The additional cost of the XSTOP device itself has to be weighed against any advantages to quality of life.

4. <u>Why have I been chosen?</u>

You are being invited to participate in this study because you suffer from Lumbar Spinal Stenosis at one or two levels in your back, and have tried to obtain symptomatic relief with previous non-surgical treatment methods, but without success.

5. <u>Do I have to take part?</u>

It is up to you to decide whether or not to take part. If you decide to take part you will be given this information sheet and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive. You may choose to have one treatment rather than the other, but if this is the case, you will not be included in the study. If significant new findings develop during the course of the study that may affect your health or willingness to participate, you will be informed.

6. <u>What is involved in the study?</u>

a. <u>What will happen to me if I take part?</u>

If you agree to take part, you would be asked to follow all the instructions given to you by the doctors, nurses and other health personnel as per routine practice in that hospital. You would be asked to visit the hospital 6 times during the 2 year follow-up period.

At your initial visit, the doctor would review your medical history including the nature of your back pain to make sure that your participation meets the study requirements. If you agree, are eligible to participate and have signed the Informed Consent Form, your doctor will enrol you into the study. Randomisation envelopes will be opened by your doctor on the day prior to surgery. This means that you only then will be assigned to either the Laminectomy-treatment group or the XSTOP-device treatment group. Until those randomisation envelopes are opened, neither your doctor nor you will know to which group you will be assigned.

If you wish to withdraw from the study you have the right to do so at any time, in which case your treatment will not be affected in any way.

b.<u>What will I be required to do?</u>

b1. Pre-operative assessments:

The following information would be discussed and recorded for both treatment groups pre-operative:

- Your initials, date of birth, weight and height
- Your diagnosis and relevant medical history
- Diagnostic measures including:
- CT (=**C**omputerised **T**omography) scan of your spine: - the CT-machine takes a lot of picture of your spine from different angles. The CT scan of your spine will only be done during this study if you do not have previous CT images, CT images

taken long time ago or the surgeon believes that the existing CT images are unsatisfactory and need repeating.

AND/OR:

- MRI(=**M**agnetic **R**esonance **I**mage) scan of your spine: - the MRI-machine produces high quality images of the spinal cord and the surrounding nerves, discs and ligaments.
- CT Myelogram (this investigation will be performed only if unable to get an MRI of your spine because of any existing contraindications e.g. pacemaker). - this procedure is the same as for getting a CT of your spine (described above) with an additional procedure of receiving an injection of a small amount of liquid contrast through a small catheter placed in your spinal canal to enhance the picture.

All the above investigations and documentation is part of routine clinical practice, whether you are part of this study or not. The following questionnaires are for patients who agree to take part in this study:

- Your doctor will go over the Inclusion and Exclusion criteria with you to see if you qualify to participate in this study.
- You will be asked to rate your average back pain level over the past week on a scale of 0-10 (VAS).
- You will be asked to complete the following 5 questionnaires about your activity level and quality of life:

- QuebecBack Pain Disability Scale(QBPDS) - -to assess your quality of life

- EQ5D – to assess your general health and well being
- SF36 - to assess your general health and well being
- Oswestry Disability Index (ODI) – to assess pain disability due to Lumbar Spinal Stenosis
- Zurich Claudication Questionnaire (ZCQ) – to check pain disability due to Lumbar Spinal Stenosis

The total time to fill in all the questionnaires should be on average 10-20 minutes. If you would like, a member of the medical team will be available to read and explain the questionnaires to you.

b2. Treatment Procedure:

The following information would be reported at time of the operation as per routine clinical practice:

- Assigned operation
- Amount of blood loss
- Duration of procedure
- All procedures performed will be documented
- Implant information (if assigned to the XSTOP-group) e.g. size of the implant used
- Intra-operative complications if any

b3. Follow-up assessments on the following visits: 7 days, 6 weeks, 6 months, 12 and 24 months:

The following information would be reported at the above mentioned time-points:

- The length of your hospital stay
- X-rays: will be performed as per hospital standard practice.

The following questionnaires (same as in Section 6(b1)) are for patients who agree to take part in this study:

- You will be asked to rate your average back pain level over the past week on a scale of 0-10 on Visual Analogue Scale(VAS).
- You will again be asked to complete the following 5 questionnaires about your activity level and quality of life:
  - EQ5D

- QBPDS
- SF 36
- Oswestry Disability Index (ODI)
- Zurich Claudication Questionnaire (ZCQ)

7. Which are the procedures that are being examined?

A. *LUMBAR LAMINECTOMY Treatment group*

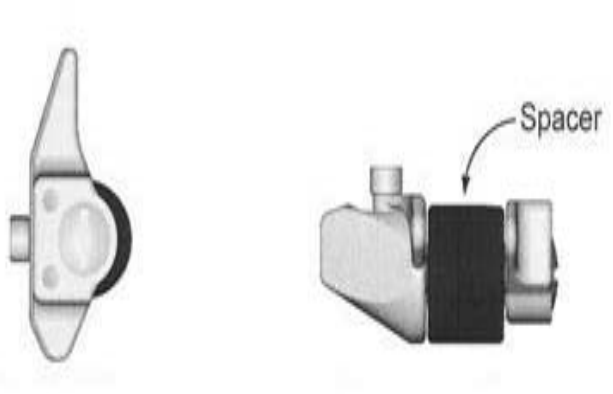
Lumbar laminectomy is a relatively safe operation where some bone and soft tissues (ligaments) are removed to free up space in the spinal canal and foramina (the opening where the nerve roots exit the spine). This way the pressure on the spinal cord and nerve roots decreases and will result in symptom relief.

Procedure:

The patient lies in face-down position under general anaesthesia. An incision is made and the spine is dissected to the level where the decompression will be performed. Decompression of the spinal cord and nerve(s) will be done by removing some parts of the bone of the spine causing the compression. As a result the pressure on the nerve roots decreases which will result in relief of symptoms.

B. *XSTOP Implant Treatment group:*

The XSTOP is a metal implant (see Fig 10.1) that fits between the two bony processes of the spine and away from the spinal cord and nerves.



Side View *Top View*

Fig 10.1: The image of the XSTOP

This is a minimally invasive surgical procedure, during which the device is generally implanted under local anaesthesia (with you awake) or general anaesthesia (with you asleep under general anaesthetic) and by a minimal open approach to your back at no more than 2 disc levels. The beneficial effect of the XSTOP implant is based on the fact that it will widen the spinal canal hence free up space for the compressed spinal cord and nerves to decompress.

Procedure:

The patient is positioned on the side, or face down. An incision is made and the XSTOP implant is placed in the created space between the bony processes of the spine. If applicable, a second XSTOP will be placed in a similar manner at a neighbouring level. This way the spinal canal and the openings where the nerves exit the spine are widened. This pressure-reduction should result in pain relief.

8. <u>What are known risks of the study or the side effects of any treatment received?</u>

<u>General Surgical Risk assessment:</u>

There are two categories of risk factors to consider here, namely that associated with general spinal surgery and also that associated with any specific surgical procedures linked to the instrumentation (surgical tools used for performing the procedure) being used.

General risks include anaesthetic-related problems, circulatory problems, a collapsed lung, pneumonia, blood clots, intra-operative damage to blood vessels, soft tissue, or nerves or an allergic reaction to blood products or medications such as antibiotics and anaesthetic agents. In very rare instances, heart attack or death may occur.

Specific risks to XSTOP are very rare and include migration of the implant (1%), malpositioning of the implant (1%), migration of the implant (1%), fracture of a part of the, bony process(1%), increased pain at implant level (1%).

Some specific risks to Lumbar Laminectomy again are rare and include the Spinal fluid leak, infection, recurrence of symptoms.

Although these complications are extremely rare, they may require additional surgery, extend the duration of surgery or extend the duration of the hospital stay. Damage to the spinal cord, usually limited to Spinal fluid leak, can occur rarely during surgery, especially where fine dissection of bone is required for decompression.

<u>Pregnancy *(relevant to female patient participants):*</u>

There is exposure to radiation from standard X-rays taken to diagnose and follow-up your spinal stenosis and the status after surgery. There is also radiation exposure during surgery from the CT-scan described above. The radiation from X-rays and the CT-scan used during the surgery may be harmful to an unborn child.

Women who could become pregnant must use an effective contraceptive during the course of this study. Thus, if you are a woman who could become pregnant, you must have a pregnancy test done prior to your enrolment into the study. If your test is positive, these study tests will be cancelled, and you will not be eligible for enrolment into this study. Also breastfeeding will exclude you from participation. Any woman who finds that she has become pregnant while taking part in the study should immediately tell her doctor.

Risk study-participation:

Participation in the study per se, does not introduce any additional risk for you, because the study will follow normal routine practice used in your hospital for both procedures, in term of surgical technique, radiographic review and follow-up visits. Most hospitals already collect some form of outcome data, so the only additional inconvenience for you will be the need to complete 5 questionnaires instead of one.

9. What are the possible benefits of taking part?

General Surgical Benefit assessment:

Both operations have been shown to be effective in the treatment of lumbar spinal stenosis. The degree of benefit expected will be discussed with you by your surgeon, since this depends on other factors also.

The benefits of spinal surgery include the potential to dramatically improve a patient's quality of life by enabling them to become more active and take a more constructive part in society. This is achieved by the removal of the cause of their pain and through rehabilitation reduces their dependence on the medical system for long term medical treatment. Obviously the level of improvement is linked to the other pre-existing medical conditions.

Benefit study-participation:

The only benefit for you from participation in the study is linked to the data collection and regular review, which could identify any potential problems earlier. You will also have an additional point of contact with regard to your condition. That contact would be the research fellow who is a neurosurgeon in training especially employed for this study who will be contactable at any time (this depends on the site involved).

10. Payment for participation

You will not be paid for participation in this study.

11. Costs for participation

No costs for study participation will be passed on to you.

12. Confidentiality

Your privacy and all personal health information will remain confidential and will not be released without your written permission to the extent permitted by law. You are giving permission to you doctor to enter data regarding your treatment and physical status into a database. The information gathered will not include your name. Your data will be identified by an assigned identification number and your initials. The anonymous database information may be analyzed to identify trends that may be used in scientific publications or presentations. Any publication of data will not identify you in any way.

The custodian of the data will be UCLH Foundation Trust, and Mr. David Choi (Consultant Neurosurgeon and the Chief Investigator for this study) will be responsible for the security of the data. The data will not be stored for longer than 10 years.

By signing this consent form, you give permission for the release of the information gathered from your participation in the study to the funding Company (Kyphon), for possible publication by Mr. Choi and / or other doctors participating in this study. Your medical records may also be reviewed by representatives of the funding company (Kyphon), by the Institutional Review Board / Ethics Committee and by representatives of the FDA or other regulatory representatives for the purpose of verifying medical information relating to this study. In addition, your doctors and other study staff at the hospital may review your medical records to collect the appropriate data for the study. The data collected in this study may be submitted to the FDA, published in medical journals, and/or presented at physician meetings. The privacy and confidentiality of your individual records will be strictly maintained as per Data Protection Act.

Data may be transmitted outside the European Union.

Your general practitioner will be informed if you decide to take part in the study. We will not inform your GP if you do not want us to do so.

13. <u>What happens if something goes wrong?</u>

In case you have any concern or complaint about any aspect of this clinical trial, you should ask to speak with the project's Chief Investigator, Mr. Choi (Tel. 020-7837-3611, Extension 3395 - Mr. Choi's secretary) who will do his best to answer your questions.

If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms will be available to you. Details are to be obtained from the hospital.

14. Who is organising and funding the research?

This is a multicentre, non-commercial study which will run at the National Hospital for Neurology and Neurosurgery (London), St Georges Hospital (London) and the Leeds General Infirmary (Leeds). This study is funded by the Kyphon Europe.

15. Withdrawal form the project

Your participation in the trial is entirely voluntary. You are free to decline, to enter or to withdraw form the study any time without having to give a reason. If you choose not to enter the trial, or to withdraw once entered, this will in no way affect your future medical care.

All information regarding your medical records will be treated as strictly confidential and will only be used for medical purposes. Your medical records may be inspected by competent authorities and properly authorised persons, but if any information is released this will be done in a coded form so that confidentiality is strictly maintained. Participation in this study will in no way affect your legal rights.

16. Who has reviewed the study?

The study was reviewed and approved by the Internal Review Panel at the National Hospital for Neurology and Neurosurgery, London as well as the Charing Cross Research Ethics Committee.

17. Contacts for further information

If you have any further questions about the study, *the investigators within your hospital* would be delighted to answer them for you.

The investigators for various sites are:

The National Hospital for Neurology and Neurosurgery

Chief Investigator - Mr David Choi MBChB, MA, PhD FRCS FRCS(SN)

Consultant Neurosurgeon and Spinal Surgeon

Victor Horsley Department of Neurosurgery

Research Fellow - Mr Besnik Nurboja BSc MBBS IMRCS

Victor Horsley Department of Neurosurgery

St Georges Healthcare NHS Trust

Principal Investigator - Mr Francis Johnston MBBS FRCS FRCS(SN)

Consultant Neurosurgeon and Spinal Surgeon

If you wish to seek independent advice or assistance you may contact the Patient Advice and Liason Service (PALS) at the hospital where you were treated.

10.4. *GP Information Sheet*

Version 1.0

30 January 2007

Cost Effectiveness & Quality of Life after Treatment of Lumbar Spinal Stenosis with the XSTOP$^{PK®}$ IPD Device or Surgical Decompression: A Prospective Randomised trial (Protocol Number – 07/X01)

Dear Dr,

Your patient ……..

D.O.B…… ……

address……

has agreed to take part in the above study.

Background to the study

Lumbar spinal stenosis (LSS) is a common and debilitating condition which consumes large amounts of healthcare resource. It occurs in 13-14% of patients who consult a specialist with back-pain, and is a considerable drain on NHS resources.

Degenerative changes in the facet joints and ligamentum flavum cause narrowing of the spinal canal and compression of nerve roots. This results in a debilitating pain or heaviness in the legs that is aggravated by walking, thereby limiting mobililty. There have been an increasing number of treatments for LSS over the years, including physiotherapy, conventional surgery (eg. lumbar laminectomy) and implantation of devices called interspinous distractors. Lumbar laminectomy and interspinous distraction are both effective methods for treatment of LSS but there is little known about the relative cost effectiveness of these treatments and quality of life for patients after treatment.

Both the conventional operation of lumbar laminectomy and the newer XSTOP device are relatively safe operations and have both been shown to be effective treatments. However, we need to establish whether there is a difference in the operative times, degree of back-pain after the operations, length of hospital stay, or complication rate between the procedures. The additional cost of the XSTOP device itself has to be weighed against any advantages to quality of life. This constitutes the basis for this study, which is sponsored by St Francis Medical Technologies Inc/ Kyphon.

What will be involved?

Your patient has symptomatic LSS and has agreed to take part in the study. They will be randomly allocated to have either the conventional lumbar laminectomy (and equivalent surgeries), or the insertion of the XSTOP device.

Aftercare and follow-up arrangements will be the same, regardless of the treatment they receive. They will be reviewed in the out-patient clinic for 2 years following surgery.

What are the benefits to taking part?

Both operations have been shown to be effective in the treatment of lumbar spinal stenosis. The degree of benefit expected will be discussed individually, since this also depends on individual symptoms and patient factors.

Further questions?

If you have any further questions about the study, we would be delighted to answer them for you. Please contact Mr David Choi via the National Hospital for Neurology and Neurosurgery. [redacted]

This study has been reviewed by the Research Ethics Committee.

10.4.CASE REPORT FORMS

Version 1.0

Date: 10/04/2008

CONTENTS

Page number

COST EFFECTIVENESS OF LUMBAR LAMINECTOMY VS XSTOP

CASE REPORT FORM (CRF 1)

CENTRE: …….

PATIENT HOSPITAL NUMBER……

PATIENT ID……

PATIENT SELECTION

Inclusion Criteria

☐ **is a male or non pregnant female patients**

☐ **is aged between 18-80 years (inclusive)**

☐ **has a BMI <35 kg/m^2**

☐ **has a preoperative ODI>30 points and a ZCQ-Physical Function Domain > 2**

☐ **has chronic leg pain with or without back pain of greater than 6 months duration improved by flexion, and who are suitable candidates for posterior lumbar surgery**

☐ **has completed at least 6 months of conservative treatment without obtaining adequate symptomatic relief**

☐ **has degenerative changes at 1 or 2 adjacent levels between L1-S1 confirmed by X-Ray, CT or MRI scan with one or more of the following:**

☐ **is physically and mentally willing and able to comply with the postoperative scheduled clinical and radiographic evaluations.**

☐ **none of the above**

Exclusion Criteria

☐ **fixed motor deficit**

☐ **is skeletally immature**

☐ **has undergone previous lumbar spinal surgery which could affect the trial outcome (e.g., disc replacement)**

☐ **has obvious signs of psychological[iii] or worker compensation or litigation claims elements to their condition**

☐ **is unwilling or unable to give consent or adhere to the follow-up programme**

☐ **has active infection or metastatic disease**

☐ **has non-degenerative spondylolisthesis**

☐ **has degenerative spondylolisthesis ≥ Meyerding Grade 2**

☐ **has a known allergy to implant materials**

☐ **has severe osteoporosis or rheumatoid arthritis**

☐ **cauda equina syndrome**

☐ **none of the above**

ELIGIBLE/ NON-ELIGIBLE (please circle one)

COST EFFECTIVENESS OF LUMBAR LAMINECTOMY VS XSTOP

CASE REPORT FORM (CRF 2)

CENTRE: …….

PATIENT HOSPITAL NUMBER……

PATIENT ID……

EPIDEMIOLOGICAL/DEMOGRAPHIC DATA

DOB: ____ /____ / _____

AGE:

GENDER: **Male** ☐ **Female** ☐

ETHNICITY: **Afro-Carribean** ☐ **White (British)** ☐

Asian ☐ **White (Other)** ☐

Middle Eastern ☐

Oriental ☐

JOB: _____

OTHER MH: _____

_____

_____

EPIDURAL INJECTION: ☐ **YES** ☐ **NO**

If YES: Date(s)_____

MEDICATION:

ASA SCORE: I II III IV V

(circle one)

COST EFFECTIVENESS OF LUMBAR LAMINECTOMY VS XSTOP

CASE REPORT FORM (CRF 3)

CENTRE: …….

PATIENT HOSPITAL NUMBER……

PATIENT ID……

CLINICAL FEATURES (pre-operatively)

	Leg		**Buttock**		**Back**		**Dermatome /Myotome**
	Yes	**No**	**Yes**	**No**	**Yes**	**No**	
Pain							
Duration (months)							
Paraesthesia							
Duration (months)							
Weakness							
Duration (months)							

COST EFFECTIVENESS OF LUMBAR LAMINECTOMY VS XSTOP

CASE REPORT FORM (CRF 4)

CENTRE: …….

PATIENT HOSPITAL NUMBER……

PATIENT ID……

PREOPERATIVE IMAGING

CT Lumbar	☐	**Date: ___/___/__**
MRI Lumbar	☐	**Date: ___/___/__**
CT Myelogram	☐	**Date: ___/___/__**
X rays	☐	**Date: ___/___/__**

Lumbar Spinal Stenosis confirmed **please tick**

L1/2	**……..**	☐
L3/4	**……**	☐
	……	☐
L4/5	**……**	☐

CASE REPORT FORM (CRF 5)

CENTRE: …….

PATIENT HOSPITAL NUMBER……

PATIENT ID……

PERIOPERATIVE OUTCOME

LSS surgery date **___/___/__**

☐ **Lumbar laminectomy?** **Number of levels _____**

☐ **XSTOP?** **Number of implants _____**

Theatre time: ____ Number of surgeons _____

Surgeons time ____ Anaesthetist time _____

Blood loss: _____ Blood transfusion: _____(no. of units)

Please state the complications

Intraoperative complications	**Early (<48hrs) complications**

CASE REPORT FORM (CRF 6)

CENTRE: …….

PATIENT HOSPITAL NUMBER……

PATIENT ID……

DISCHARGE OUTCOME

Discharged? Yes No

Date of Discharge: ____/ ___/____ Inpatient stay (no.of days)_____

VAS (back) 1 2 3 4 5 6 7 8 9 10

VAS (leg) 1 2 3 4 5 6 7 8 9 10

Total analgesia: NSAIDS _____

Opioids

- **p.o._____**
- **i.m.**

Total physiotherapy episodes: _____

Post-op X rays Yes No

(AP, Flex/Ext)

CASE REPORT FORM (CRF 7)

CENTRE: …….

PATIENT HOSPITAL NUMBER……

PATIENT ID……

PATIENT ASSESSMENT: 6 weeks 6 months 12months 24 months

(circle one)

CLINICAL FEATURES (post-operatively)

	Leg		**Buttock**		**Back**		**Dermatome**
	Yes	**No**	**Yes**	**No**	**Yes**	**No**	**/Myotome**
***Pain**							
Duration							
Paraesthesia							
Duration							
Weakness							
Duration							

* If you tick response Yes for Pain please include the VAS score.

CASE REPORT FORM (CRF 8)

(see 5 subforms)

CENTRE: …….

PATIENT HOSPITAL NUMBER……

PATIENT ID……

PATIENT ASSESSMENT: Preop Discharge (EQ5D, ZCQ Symptoms component) 6 weeks 6 months 12months 24 months

(circle one)

OUTCOME QUESTIONNAIRES

OUTCOME QUESTIONNAIRE SCORES & IMAGING

QBPDS(see CRF 7 -1) _____

EQ5D (see CRF 7 -2)

- Mobility __ Self-care__ Usual activities__ Pain/Discomfort__ Anxiety/Depression___

- Total score: ☐☐☐☐ **- Health state: _____**

ODI (see CRF 7-3)

_____% (10 parts, each part score 0 – 5, final score(%) = total score/50 x 100%)

ZCQ Symptom Severity ___ Physical Function____ Satisfaction scale____

SF36 (see CRF 7- 5) PF__ RP__ BP__ GH___ VT__ SF__ RE___ MH___

X rays Yes No

(AP, Flex/Ext)

X rays Satisfactory:Yes

CASE REPORT FORM (CRF 8-1)

CENTRE: …….

PATIENT HOSPITAL NUMBER……

PATIENT ID……

PATIENT ASSESSMENT: PREOP 6 weeks 6 months 12months 24 months

(circle one)

10.6.The Quebec Back Pain Disability Scale

This questionnaire is about the way your back pain is affecting your daily life. People with back problems may find it difficult to perform some of their daily activities. We would like to know if you find it difficult to perform any of the activities listed below, because of your back. For each activity there is a scale from 0 to 10

(0, not difficult at all; 5, moderately difficult; 10, extremely difficult).

Please choose one response option for each activity (please do not skip any activity) and circle the corresponding number.

Today, do you find it difficult to perform the following activities because of your back?

1. Get out of bed ……0 1 2 3 4 5 6 7 8 9 10
2. Sleep for at least 6 hours ……0 1 2 3 4 5 6 7 8 9 10
3. Turn over in bed ……0 1 2 3 4 5 6 7 8 9 10
4. Travel 1 hour in a car……..0 1 2 3 4 5 6 7 8 9 10
5. Stand up for 20-30 minutes……0 1 2 3 4 5 6 7 8 9 10
6. Sit in a chair for several hours……0 1 2 3 4 5 6 7 8 9 10
7. Climb one flight of stairs……0 1 2 3 4 5 6 7 8 9 10

8. Walk a few blocks (300-400 m)……. 0 1 2 3 4 5 6 7 8 9 10
9. Walk several miles……..0 1 2 3 4 5 6 7 8 9 10
10. Reach up to high shelves…….0 1 2 3 4 5 6 7 8 9 10
11. Throw a ball……0 1 2 3 4 5 6 7 8 9 10
12. Run two blocks……0 1 2 3 4 5 6 7 8 9 10
13. Take food out of the refrigerator…….0 1 2 3 4 5 6 7 8 9 10
14. Make your bed……0 1 2 3 4 5 6 7 8 9 10
15. Put on socks (pantyhouse)…….. 0 1 2 3 4 5 6 7 8 9 10
16. Bend over a sink for 10 minutes……..0 1 2 3 4 5 6 7 8 9 10
17. Move a table……0 1 2 3 4 5 6 7 8 9 10
18. Pull or push heavy doors…….0 1 2 3 4 5 6 7 8 9 10
19. Carry two bags of groceries……0 1 2 3 4 5 6 7 8 9 10
20. Lift 40 lbs (heavy suitcase)……. 0 1 2 3 4 5 6 7 8 9 10

CASE REPORT FORM (CRF 8-3)

CENTRE: …….

PATIENT HOSPITAL NUMBER……

PATIENT ID……

PATIENT ASSESSMENT: PREOP 6 weeks 6 months 12months 24 months

(circle one)

10.7.OSWESTRY DISABILITY INDEX

(Fairbank JCT, Pynsent PB. The Oswestry Disability Index. Spine 2000;25:2940–53.)

Please Read: This questionnaire is designed to enable us to understand how much your low back has affected your ability to manage everyday activities. Please answer each Section by circling the ONE CHOICE that most applies to you. We realize that you may feel that more than one statement may relate to you, but **please just circle the one choice which closely describes your problem right now.**

SECTION 1—Pain Intensity

A. I can tolerate the pain I have without having to use painkillers
B. The pain is bad but I can manage without painkillers.
C. Painkillers give complete relief from pain
D. Painkillers give moderate relief from pain
E. Painkillers give very little relief from pain
F. Painkillers have no effect on the pain and I do not use them

SECTION 2—Personal Care

A. I can look after myself normally without causing extra pain.
B. I can look after myself normally but it causes extra pain.

C. It is painful to look after myself and I am slow and careful
D. I need some help but manage most of my personal care
E. I need help every day in most aspects of self-care.
F. I do not get dressed. I wash with difficulty and stay in bed

SECTION 3 –Lifting

A. I can lift heavy weights without extra pain
B. I can lift heavy weights but it gives extra pain
C. I can't lift heavy objects from off the floor but off the table is OK.
D. I can't lift heavy objects but light to medium ones are OK.
E. I can only lift very light weights
F. I cannot lift or carry anything at all.

SECTION 4 – Walking

A. Pain does not prevent me from walking any distance.
B. Pain prevents me from walking more than one mile.
C. Pain prevents me from walking more than one-half of mile.
D. Pain prevents me from walking more than one-quarter of mile.
E. I can only walk while using a cane or on crutches
F. I am in bed most of the time and have to crawl to the toilet.

SECTION 5 – Sitting

A. I can sit in any chair as long as I like without pain
B. I can only sit in my favourite chair as long as I like.
C. Pain prevents me from sitting more than one hour
D. Pain prevents me from sitting more than ½ hour
E. Pain prevents me from sitting more than ten minutes.
F. Pain prevents me from sitting at all.

SECTION 6 – Standing

A. I can stand as long as I want without extra pain.
B. I can stand as long as I want but it gives extra pain
C. Pain prevents me from standing for more than one hour

D. Pain prevents me from standing for more than 30 minutes
E. Pain prevents me from standing for more than 10 minutes
F. Pain prevents me from standing at all

SECTION 7 – Sleeping

A. Pain does not prevent me from sleeping well
B. I can sleep well only by using tablets
C. Even when I take tablets I have less than six hours of sleep
D. Even when I take tablets I have less than four hours of sleep
E. Even when I take tablets I have less than two hours of sleep
F. Pain prevents me from sleeping at all.

SECTION 8 – Sex Life

A. My sex life is normal and causes no extra pain.
B. My sex life is normal but causes some extra pain.
C. My sex life is nearly normal but is very painful.
D. My sex is severely restricted because of pain.
E. My sex life is nearly absent because of pain.
F. Pain prevents any sex life at all.

SECTION 9 – Social Life

A. My social life is normal and gives me no extra pain.
B. My social life is normal but increases the degree of pain
C. I can't participate in more energetic activities like dancing or tennis
D. Pain restricts my social life and I don't go out as often.
E. Pain restricts my social life at home.
F. I have no social life because of pain.

SECTION 10 – Travelling

A. I can travel anywhere without pain.
B. I can travel anywhere but it gives me extra pain.
C. Pain is bad but I manage journeys over two hours.
D. Pain restricts me to journeys of less than one hour.

E. Pain restricts me to short necessary journeys of less than 30 minutes.

F. Pain prevents me from travelling.

CASE REPORT FORM (CRF 8-4)

CENTRE: …….

PATIENT HOSPITAL NUMBER……

PATIENT ID……

PATIENT ASSESSMENT: PREOP 6 weeks 6 months 12months 24 months

(circle one)

10.8.**ZURICH CLAUDICATION QUESTIONNAIRE**

Please Read: This questionnaire has been designed to give the doctor information as to how your back pain has affected your ability to manage in everyday life. Please answer every section by circling the ONE CHOICE that most applies to you. We realize you may consider that two of the statements in any one section relate to you, but please just circle the one choice *which* most closely describes your problem.

PART l: - Symptom Severity Scale

In the last month, how would you describe:

Question 1. The pain you have had on average including the pain in you back, buttocks and pain that goes down your legs?

1. **None**
2. **Mild**
3. **Moderate**
4. **Severe**
5. **Very severe**

Question 2. How often have you had back, buttock, or leg pain?

1. **Less than once a week**
2. **At least once a week**
3. **Everyday, for at least a few minutes**

4. **Everyday, for most of the day**
5. **Every minute of the day**

Question 3. The pain in your back or buttocks?

1. **None**
2. **Mild**
3. **Moderate**
4. **Severe**
5. **Very severe**

Question 4. The pain in your legs or feet?

1. **None**
2. **Mild**
3. **Moderate**
4. **Severe**
5. Very severe

Question 5. Numbness or tingling in your legs or feet?

1. **None**
2. **Mild**
3. **Moderate**
4. **Severe**
5. **Very severe**

Question 6. Problems with your balance?

1. **No, I have had no problems with balance**
2. **Yes, sometimes I feel my balance is off, or that I am not sure footed**
3. **Yes, often I feel my balance is off, or that I am not sure footed**

Question 7. Weakness in your legs or feet?

1. None
2. Mild
3. Moderate
4. Severe

5. Very Severe

PART 2: - Physical Function Scale

In the last month, on a typical day;

Question 8. How far have you been able to walk?

1. **Over 2 miles**
2. **Over 2 blocks, but les than 2 miles**
3. **Over 50 feet, but less than 2 blocks**
4. **Less than 50 feet**

Question 9. Have you taken walks outdoors or in the shopping centres?

1. **Yes, comfortably**
2. **Yes, but sometimes with pain**
3. **Yes, but always with pain**
4. **No**

Questio 10. Have you been shopping for groceries or other items?

1. Yes, comfortably
2. Yes, but sometimes with pain
3. Yes, but always with pain
4. No

Question 11. Have you walked around the different rooms in your house or apartment?

1. **Yes, comfortably**
2. **Yes, but sometimes with pain**
3. **Yes, but always with pain**
4. **No**

Question 12. Have you walked from your bedroom to the bathroom?

1. **Yes, comfortably**
2. **Yes, but sometimes with pain**
3. **Yes, but always with pain**
4. **No**

Part 3: - Satisfaction Scale

How satisfied are you with:

Question 13. The overall result of back operation

1. Very satisfied

2. Somewhat satisfied

3. Somewhat dissatisfied

4. Very dissatisfied

Question 14. Relief of pain following the operation?

1. **Very satisfied**
2. **Somewhat satisfied**
3. **Somewhat dissatisfied**
4. **Very dissatisfied**

Question 15. Your ability to walk following the operation

1. **Very satisfied**
2. **Somewhat satisfied**
3. **Somewhat dissatisfied**
4. **Very dissatisfied**

Question 16. Your ability to do housework, yard work, or job following the operation?

1. **Very satisfied**
2. **Somewhat satisfied**
3. **Somewhat dissatisfied**
4. **Very dissatisfied**

Question 17. Your strength in the thighs, legs and feet?

1. **Very satisfied**
2. **Somewhat satisfied**
3. **Somewhat dissatisfied**
4. **Very dissatisfied**

Question 18. Your balance or steadiness on your feet?

1. **Very satisfied**
2. **Somewhat satisfied**
3. **Somewhat dissatisfied**
4. **Very dissatisfied**

CASE REPORT FORM (CRF 8-2)

CENTRE: …….

PATIENT HOSPITAL NUMBER……

PATIENT ID……

PATIENT ASSESSMENT: Preop Discharge 6 wks 6 mths 12mths 24mths

(circle one)

10.9.EQ5D

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today

Mobility

I have no problems in walking about

I have some problems in walking about

I am confined to bed

Self-Care

I have no problems with self-care

I have some problems washing or dressing myself

I am unable to wash or dress myself

Usual activities (e.g. work, study, housework, family or

Leisure activities)

I have no problems with performing my usual activities

I have some problems with performing usual activities

I am unable to perform my usual activities

Pain/Discomfort

I have no pain or discomfort

I have moderate pain or discomfort

I have extreme pain or discomfort

Anxiety/Depression

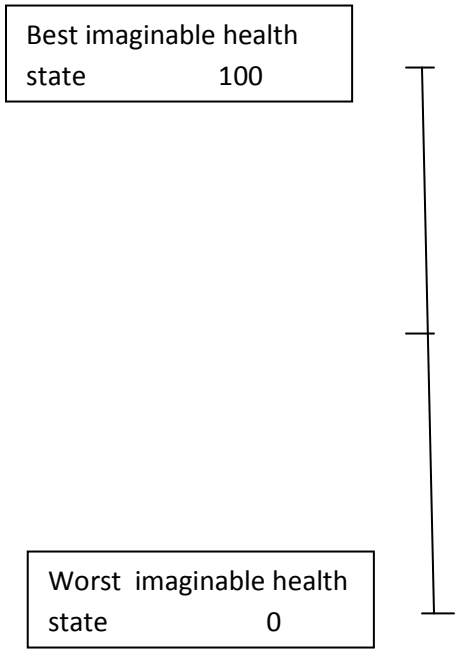
I am not anxious or depressed

I am moderately anxious or depressed

I am extremely anxious or depressed

EQ5D VAS

Best Imaginable Health State – We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.



COST EFFECTIVENESS OF LUMBAR LAMINECTOMY VS XSTOP

CASE REPORT FORM (CRF 8-5)

CENTRE: …….

PATIENT HOSPITAL NUMBER……

PATIENT ID……

PATIENT ASSESSMENT: Preop 6 wks 6 mths 12mths 24 mths

(circle one)

10.10.*SF-36*

INSTRUCTIONS: This survey asks your vies about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.

Answer every question by marking the answer as indicated. If you are unsure about how to answer a question, please give the best answer you can.

1. In general, would you say your health is: (circle one)

Excellent…… 1

Very good ……..2

Good ……..3

Fair……4

Poor……5

2.Compared to one year ago, how would you rate your health in general now?

(circle one)

Much better now than one year ago ……1

Somewhat better now than one year ago……2

About the same as one year ago……3

Somewhat worse now than one year ago……4

Much worse now than one year ago……5

3.The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

(circle a number on each line)

ACTIVITIES	***Yes, limited a lot***	***Yes, limited a little***	***No, not limited at all***
Vigorous activity, such as running, lifting heavy objects, participating in strenuous sports	***1***	***2***	***3***
Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	***1***	***2***	***3***
Lifting or carrying groceries	***1***	***2***	***3***
Climbing several flights of stairs	***1***	***2***	***3***
Climbing one flight of stairs	***1***	***2***	***3***
Bending, kneeling, or stooping	***1***	***2***	***3***
Walking more than a mile	***1***	***2***	***3***
Walking half a mile	***1***	***2***	***3***
Walking 100 yards	***1***	***2***	***3***
Bathing or dressing yourself	***1***	***2***	***3***

4.During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

(circle one number on each line)

	YES	***NO***
a. Cut down on the amount of itme you spent on work or other activities	***1***	***2***
b. Accomplished less than you would like	***1***	***2***
c. Were limited in the kind of work or other activities	***1***	***2***
d. Had difficulty performing the work or other activities (for example, it took extra effort)	***1***	***2***

5.During the past 4 weeks have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

(circle one number on each line)

	YES	***NO***
a. Cut down the amount of time you spent on work or other activities	***1***	***2***
b. Accomplished less than you would like	***1***	***2***
c. Didn't do work or other activities as carefully as usual	***1***	***2***

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups?

(circle one)

Not at all……1

Slightly……2

Moderately……3

Quite a bit……4

Extremely……5

7. How much bodily pain have you had during the past 4 weeks?

(circle one)

None……1

Very mild……2

Mild……3

Moderate……4

Severe……5

Very severe……6

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

(circle one)

Not at all……1

A little bit……..2

Moderately……3

Quite a bit……4

Extremely……5

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks –

(circle one)

	All of the time	*Most of the time*	*A good bit of time*	*Some of the time*	*A little of the time*	*None of the time*
a. Did you feel full of life	*1*	*2*	*3*	*4*	*5*	*6*
b. Have you been a very nervous person	*1*	*2*	*3*	*4*	*5*	*6*
c. Have you felt so down that nothing could cheer you up	*1*	*2*	*3*	*4*	*5*	*6*
d. Have you felt calm and peaceful?	*1*	*2*	*3*	*4*	*5*	*6*
e. Did you have a lot of energy	*1*	*2*	*3*	*4*	*5*	*6*
f. Have you felt downhearted and low?	*1*	*2*	*3*	*4*	*5*	*6*
g. Did you	*1*	*2*	*3*	*4*	*5*	*6*

feel worn out?						
h. Have you been a happy person?	***1***	***2***	***3***	***4***	***5***	***6***
i. Did you feel tired?	***1***	***2***	***3***	***4***	***5***	***6***

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc)?

(circle one)

All of the time……1

Most of the time……2

Some of the time……3

A little of the time……4

None of the time……5

11. How TRUE or FALSE is each of the following statements for you?

(circle one number on each line)

	Definitely True	***Mostly True***	***Don't Know***	***Mostly False***	***Definitely False***
a. I seem to get ill a little easier	***1***	***2***	***3***	***4***	***5***

than other people					
b. I am as healthy as anubody I know	***1***	***2***	***3***	***4***	***5***
c. I expect my health to get worse	***1***	***2***	***3***	***4***	***5***
d. My health is excellent	***1***	***2***	***3***	***4***	***5***