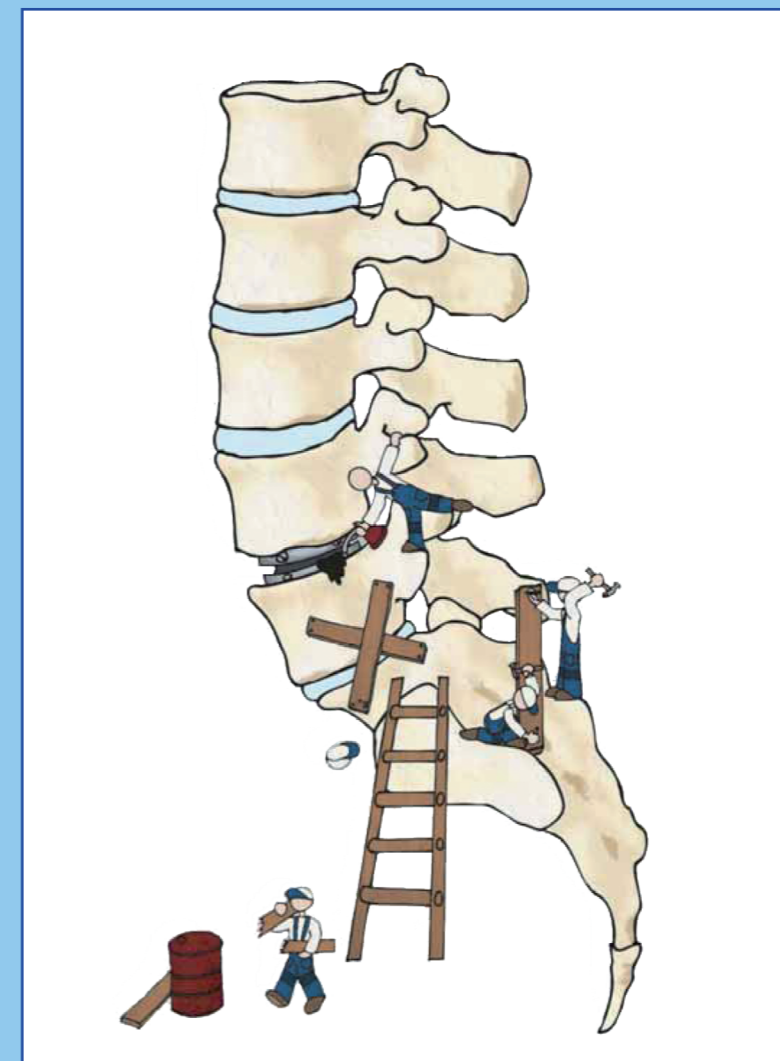


# *Acta Orthopaedica*

## **On total disc replacement**

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# On total disc replacement

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**Linköping University**  
FACULTY OF HEALTH SCIENCES

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## Abstract

Low back pain consumes a large part of the community's resources dedicated to health care and sick leave. Back disorders also negatively affect the individual leading to pain suffering, decreased quality-of-life and disability. Chronic low back pain (CLBP) due to degenerative disc disease (DDD) is today often treated with fusion when conservative treatment has failed and symptoms are severe. This treatment is as successful as arthroplasty is for hip arthritis in restoring the patient's quality of life and reducing disability. Even so, there are some problems with this treatment, one of these being recurrent CLBP from an adjacent segment (ASD) after primarily successful surgery. This has led to the development of alternative surgical treatments and devices that maintain or restore mobility, in order to reduce the risk for ASD. Of these new devices, the most frequently used are the disc prostheses used in Total Disc Replacement (TDR).

This thesis is based on four studies comparing total disc replacement with posterior fusion. The studies are all based on a material of 152 patients with DDD in one or two segments, aged 20-55 years that were randomly treated with either posterior fusion or TDR.

The first study concerned clinical outcome and complications. Follow-up was 100% at both one and two years. It revealed that both treatment groups had a clear benefit from treatment and that patients with TDR were better in almost all outcome scores at one-year follow-up. Fusion patients continued to improve during the second year. At two-year follow-up there was a remaining difference in favour of TDR for back pain. 73% in the TDR group and 63% in the fusion group were much better or totally pain-free (n.s.), while twice as many patients in the TDR group were totally pain free (30%) compared to the fusion group (15%).

Time of surgery and total time in hospital were shorter in the TDR group.

There was no difference in complications and reoperations, except that seventeen of the patients in the fusion group were re-operated for removal of their implants.

The second study concerned sex life and sexual function. TDR is performed via an anterior approach, an approach that has been used for a long time for various procedures on the lumbar spine. A frequent complication reported in males when this approach is used is persistent retrograde ejaculation. The TDR group in this material was operated via an extra-peritoneal approach to the retroperitoneal space, and there were no cases of persistent retrograde ejaculation. There was a surprisingly high frequency of men in the fusion group reporting deterioration in ability to have an orgasm postoperatively. Preoperative sex life was severely hampered in the majority of patients in the entire material, but sex life underwent a marked improvement in both treatment groups by the two-year follow-up that correlated with reduction in back pain.

The third study was on mobility in the lumbar spinal segments, where X-rays were taken in full extension and flexion prior to surgery and at two-year follow-up. Analysis of the films showed that 78% of the patients in the fusion group reached the surgical goal (non-mobility) and that 89% of the TDR patients maintained mobility.

Preoperative disc height was lower than in a normative database in both groups, and remained lower in the fusion group, while it became higher in the TDR group. Mobility in the operated segment increased in the TDR group postoperatively. Mobility at the rest of the lumbar spine increased in both treatment groups. Mobility in adjacent segments was within the norm postoperatively, but slightly larger in the fusion group.

In the fourth study the health economics of TDR vs Fusion was analysed. The hospital costs for the procedure were higher for patients in the fusion group compared to the TDR group, and the TDR patients were on sick-leave two months less.

In all, these studies showed that the results in the TDR group were as good as in the fusion group. Patients are more likely to be totally pain-free when treated with TDR compared to fusion. Treatment with this new procedure seems justified in selected patients at least in the short-term perspective. Long-term follow-up is underway and results will be published in due course.

## Abbreviations

<b>ALIF</b>	Anterior lumbar interbody fusion	<b>MRI</b>	Magnetic resonance imaging
<b>AP</b>	Anterior–posterior	<b>ns</b>	Not statistically significant
<b>ASD</b>	Adjacent segment disease	<b>ODI</b>	Oswestry Disability Index
<b>CBT</b>	Cognitive behavioural treatment	<b>ODI8</b>	Question 8 in the original Oswestry Disability Index
<b>CI</b>	Confidence interval	<b>PLF</b>	Posterolateral fusion
<b>CLBP</b>	Chronic low back pain	<b>PLIF</b>	Posterior lumbar interbody fusion
<b>CPP</b>	Cost per patient	<b>QoL</b>	Quality-of-life
<b>DCRA</b>	Distortion compensated roentgen analysis	<b>QUALY</b>	Quality adjusted life years
<b>DDD</b>	Degenerative disc disease	<b>RCT</b>	Randomised controlled trial
<b>Diff</b>	Difference	<b>ROM</b>	Range of motion
<b>EBM</b>	Evidence-based medicine	<b>SD</b>	Standard deviation
<b>EQ-5D</b>	EuroQol questionnaire based on five dimensions	<b>SEK</b>	Swedish currency “Krona”
<b>FDA</b>	Food and Drug Administration	<b>SF-36</b>	Short Form 36 Health Survey Questionnaire
<b>FUS</b>	Fusion	<b>SweSpine</b>	Swedish Spine Register
<b>GA</b>	Global assessment (of change in back pain)	<b>TDR</b>	Total disc replacement
<b>GP</b>	General practitioner	<b>US</b>	United States of America
<b>ICER</b>	Incremental cost-effectiveness ratio	<b>VAS</b>	Visual analogue scale
<b>LBP</b>	Low back pain	<b>X-ray</b>	Radiographic examination
<b>MCID</b>	Minimal clinically important difference		

## List of publications

- I. Total disc replacement compared to lumbar fusion: a randomized controlled trial with 2-year follow-up.  
Svante Berg, Tycho Tullberg, Björn Branth, Claes Olerud, Hans Tropp  
*European Spine Journal* (2009) 18:1512–1519.  
DOI 10.1007/s00586-009-1047-0
- II. Sex life and sexual function in men and women before and after total disc replacement compared with posterior lumbar fusion.  
Svante Berg, Peter Fritzell, Hans Tropp  
*The Spine Journal* (2009) 9: 987–994.  
DOI 10.1016/j.spinee.2009.08.454
- III. Disc height and motion patterns in the lumbar spine in patients treated with total disc replacement or fusion for discogenic back pain. Results from a randomized controlled trial.  
Svante Berg, Hans Tropp, Gunnar Leivseth  
Submitted for publication.
- IV. A full economic evaluation of disc prosthesis vs. lumbar fusion in patients with chronic low back pain. Randomized controlled trial with two-year follow up.  
Peter Fritzell, Svante Berg, Fredrik Borgström, Tycho Tullberg, Hans Tropp  
Submitted for publication.

## Introduction

Total disc replacement involves replacement of the intervertebral disc with an artificial articulation between the vertebral bodies. The main goal of this operation is to reduce pain, and try to restore or preserve segmental movement and stability. The main rationale is removal of the painful disc, restoration of disc height and mobility. The aim of this thesis was to see if TDR has anything to add beyond the current surgical treatment for this type of chronic LBP.

### The motion segment

Mechanically the spine consists of vertebrae connected by a mobile junction, the functional spinal unit or the motion segment<sup>15</sup>. The mobile junction has three major constituents, the two facet joints (inter-vertebral joints) between the arches of the two adjoining vertebrae, one on each side, and the intervertebral disc, creating the mobile connection between adjoining vertebral bodies. In a subgroup of all patients suffering from low back pain (LBP), the pain seems to emanate from one of the components of the functional spinal unit<sup>81</sup> having the properties of a mechanical pain.

Until now the facet joints have received the most attention regarding the source of pain<sup>93</sup> but recent research suggests the inter-vertebral disc to be the more frequent source of pain<sup>10,15</sup> and that changes in the facet joints are usually secondary.

### The medical problem is discogenic pain

The inter-vertebral disc is a highly organised matrix laid down by relatively few cells in a specific manner<sup>97,107</sup>. A degenerated disc may, but not necessarily, be painful, and structural degeneration alone does not seem to be the full explanation for this type of back pain<sup>10</sup>. Some factors leading to a painful disc are known.

Disc degeneration begins when catabolism and/or the failure to retain matrix proteins consistently exceed synthesis and/or retention<sup>1</sup>. Although many factors may contribute, the key factor is decreased nutrition in the centre of the nucleus, low pH, and possibly cell death<sup>1</sup>. Diffusion over the endplate, which is the nutritional source of the disc, is reduced with both age and degeneration<sup>114</sup>. Changes in cell biology may precede critical changes<sup>1</sup>.

The reason why a degenerated disc becomes painful is not fully understood. There are however various theories. One of these is that the outer annulus or “peri-discal membrane”, equipped with a rich sensory innervation, is the structure signalling pain<sup>97</sup>. The question is: why do these structures with

their nerve-terminals suddenly start to signal pain? Since disc degeneration is a prerequisite for this form of pain, it is possible that the accompanying dehydration and loss of disc height causes the disc to move abnormally when loaded. Stretching and tension at the disc surface is then registered in these nerve-terminals<sup>97,150</sup>.

Another theory is that fissures occurring in a degenerating disc lead to an inflammatory reaction followed by invasion of small vessels and along with them nerves into the initially nerve-free disc. This theory is supported by animal studies<sup>4</sup>. This neoinnervation could signal pain, but this theory gives no explanation for any pain that might have been present before occurrence of these fissures.

The endplate, the surface of the vertebral body adjacent to the disc, has also been demonstrated to take part in the degenerative process producing pain<sup>20,97,107</sup>.

A combination of such factors is probably the explanation for the pain in this patient group as proposed by Brisby. The author furthermore points out a number of inflammatory and signaling substances present, such as tumour necrosis factor and interleukins (interleukin-1 $\beta$ , interleukin-6, and interleukin-8) and the possibility of an amplified response caused by peripheral and central sensitisation. Due to the complexity of the nervous system and pain modulation mechanisms, it is possible that psychological aspects may also play a role in the response of the nervous system in patients with chronic low-back pain caused by disc degeneration<sup>19</sup>.

Cadaver studies have shown a clear correlation between annular tears at post-mortem discography and a history of LBP<sup>140</sup>.

*Painful degenerative disc disease* (DDD) was previously attributed to an accumulation of environmental factors, such as repeated mechanical insults and injuries (a wear-and-tear phenomenon) imposed on the normal aging of the disc. Stokes and Iatridis<sup>128</sup> in their review conclude that both overload and immobilisation might contribute to the normal degenerative process in discs. Research conducted over the past decade has led to a dramatic shift in the understanding of disc degeneration and its aetiology<sup>8,25,75</sup>. Results of exposure-discordant monozygotic and classic twin studies suggest that physical loading specific to occupation and sport plays a relatively minor role in disc degeneration. Recent research indicates that heredity has a dominant role in disc degeneration, explaining 74% of the variance in adult populations studied to date. Since 1998, genetic influences have been demonstrated by the identification of several gene forms associated with disc degeneration<sup>8</sup>. This is also confirmed in other studies. These emphasise that the primary factor for development of painful DDD is genetic, and that there are differences present between genetically different populations<sup>25,75</sup>.

Smoking has also been found to be associated with increased prevalence of LBP<sup>123</sup>.

The correlation to CLBP was higher than to “recent” LBP in smokers.

Biologic treatment is under investigation in animal studies<sup>1</sup>. If successful, this may alter the natural history of disc degeneration. Biologic treatment may be limited to early stages of degeneration, before endplate alterations prevent adequate disc nutrition. Three approaches are under investigation: cellular transplantation, administration of growth factors, and gene transfer<sup>1</sup>.

## Today's treatment

Chronic low back pain (CLBP) emanating from degenerative changes in the motion segment between the lumbar vertebrae is the most frequent cause for sick leave amongst people with LBP<sup>118,119</sup>, creating severe suffering and low quality of life for many people<sup>38,119,143</sup>.

The consensus of an “evidence-based review” by van Tulder<sup>139</sup> is that patients suffering from CLBP due to DDD should always try *conservative treatment* before surgery is considered. It is well documented that conservative treatment may help in reducing pain, improving the ability to cope with the remaining pain as well as restoring working capacity<sup>52</sup>. Besides physical therapy and training, modern conservative treatment also includes cognitive behavioural therapy (CBT) and development of coping strategies<sup>21</sup>.

When conservative treatment fails surgery might be considered<sup>27,28,148</sup>. One of the indications for spinal surgery according to evidence-based medicine (EBM)<sup>35,52</sup> seems to be pain caused by DDD. The patients with DDD often present a history of mechanical low back pain varying with different body positions, movements and loads.

Even though this patient group has been the focus of many spine surgeons, the results of surgical treatment when conservative management has failed could be even better. This is partly explained by the difficulty in correct patient selection for surgery, the natural course of degenerative changes in the rest of the spine<sup>141</sup>, and by the fact that the current treatment by different fusions alters biomechanics and physiological function, inducing degenerative changes in adjacent segments of the spine.

The selection of patients likely to profit from *spinal surgery* is the most challenging task<sup>35</sup>. Diagnosis is often made by patient history (especially what increases or decreases pain), clinical findings (with localised interspinous tenderness), loss of disc height on X-ray and signs of localised disc degeneration seen on MRI<sup>35</sup>. A psychosocial evaluation of the patient in relation to their “pain-history” and functional impairment should be made<sup>42,143,146</sup>. When contemplating surgery for DDD, the surgical decision may be supported by obvious degeneration of the actual disc, as seen on T2-weighted MRI-scans. It has

recently been suggested that oedema in the bony endplate surrounding the disc (Modic sign) increases the probability of a painful disc<sup>74,135</sup>. High-intensity zones in a disc-bulge have also been shown to correlate with LBP<sup>5</sup>. Various diagnostic injections are sometimes used to localise / rule out certain anatomical structures as the cause of pain<sup>37,58,100,101,109</sup>.

The studies in this thesis have focused on proposed segmental pain due to DDD and the surgical treatment of these patients where conservative treatment has failed.

Evidence-based medicine suggests spinal fusion to be “the gold standard” to eliminate painful movement and load in the surgical treatment of chronic low back pain due to DDD<sup>35,52</sup>. Quality-of-life scores following fusion surgery have been shown to be as good as for the treatment of osteoarthritis of the hip by arthroplasty<sup>131,132</sup>. This is supported by numerous studies<sup>24</sup> of varying scientific importance. Some RCTs compared treatment of extended rehabilitation according to modern principles with surgery. Fairbank et al 2006 compared surgical treatment (fusion) with conservative treatment for DDD<sup>45</sup>. Results in that study were just barely in favour of surgical treatment. Furthermore these results are questionable since patients included were taken from a group where previous evaluation suggested little chance for successful surgery. A Norwegian RCT compared instrumented fusion to very ambitious conservative treatment including CBT<sup>21</sup>. No difference was observed between the groups. The study has been criticised for its short time of follow-up<sup>72</sup>, small groups and cross-over to surgery in 30% of the non surgically treated patients. One large RCT performed by the Swedish Spine Study Group<sup>48</sup> demonstrated results clearly in favour of surgery. This study has met criticism concerning the design of the non-surgical treatment<sup>106</sup>. It is obvious that reliable studies have proven difficult to perform<sup>115</sup>.

Different fusion techniques have been used for more than a century, for various diagnoses. Initially fusions were mostly used for fractures, deformities or infections<sup>60</sup>. Over the last fifty years different fusions have been developed with the aim of reducing symptoms in patients with painful DDD<sup>61</sup>.

In the earliest techniques used to fuse a motion segment, fixation and bony fusion between the spinal processes of two adjoining vertebrae was conducted<sup>83</sup>. Nowadays posterolateral fusion (PLF) is frequently performed, where bone graft is placed to bridge over the gap between the decorticated transverse processes together with destruction of cartilaginous surfaces of the facet joints and concomitant bone grafting. Another option is to remove the disc, decorticate the endplates and perform a fusion: a procedure called inter-corporal fusion. If this type of fusion is performed via a posterior approach it is called a PLIF (posterior lumbar interbody fusion), if from an anterior approach, an ALIF. Fusion techniques are both non-instrumented or stabilised with transpedicular screws in combination with rods or plates. The latter procedure performed to enhance fusion rate and allow for early mobilisation of the patient without a corset.

It is worth mentioning that even though the disc is considered the "pain generator", some of the above techniques leave the disc in place, while others remove the disc. Despite these differences in fusion techniques there was no difference in clinical outcome<sup>39,49</sup>. An explanation for this could be that an unloaded disc left in place but stabilised loses its capacity to generate pain.

### Problems with current surgical treatment

Fusion surgery creates its specific problems and negative side-effects.

In a study receiving the highest evidence-based ranking<sup>48</sup>, two-year results showed that 29% of the patients operated upon, regardless of method, reported total relief of pain or being much better, 63% reported improvement. These figures were twice as high as in the control group receiving conservative treatment. There was a relatively large group of patients who remained unchanged or even worse (37% in the same study).

Another potential problem in patients treated for CLBP is return of symptoms a long time after the initial treatment. As a result of successful fusion and continuous ongoing degeneration, most spine surgeons consider recurrent pain to originate from "adjacent segment disease" (ASD), a reality in some patients<sup>53,111</sup>. There is a controversy on this issue in the literature with frequency figures varying from 0% to 60%<sup>7,53,54,85,86,111</sup>. The natural course of ageing<sup>141</sup> is considered to be the major constituent in this development. Fusion surgery might enhance adjacent-segment biomechanical changes. Increased load on movement in the segment adjacent to a fusion might induce or speed up the progressive disc degeneration itself. There is more evidence for the existence of this phenomenon than against it. There are indications that age at surgery, restoration of lordosis and surgical technique affect the risk for developing ASD<sup>105</sup>. The risk for developing ASD seems to be dependent on the fusion technique<sup>40</sup>.

### The new approach to surgical treatment

Fernström, a Swedish neurosurgeon, was the pioneer of mobility preservation and maintenance of disc height in DDD and after discectomy. In the early sixties, he reported on implantation of a stainless steel ball into the disc space via a posterior approach (Figure 1a)<sup>46</sup>. However, a reduction in disc-height frequently occurred due to subsidence of the steel ball into the endplates. This led to fusion (Figure 1b), and the method was abandoned.

Numerous different implants have been developed aiming to achieve pain reduction with maintained mobility<sup>16</sup>.

The underlying idea leading to the development of Total Disc Replacement (TDR) is maintenance or restoration of

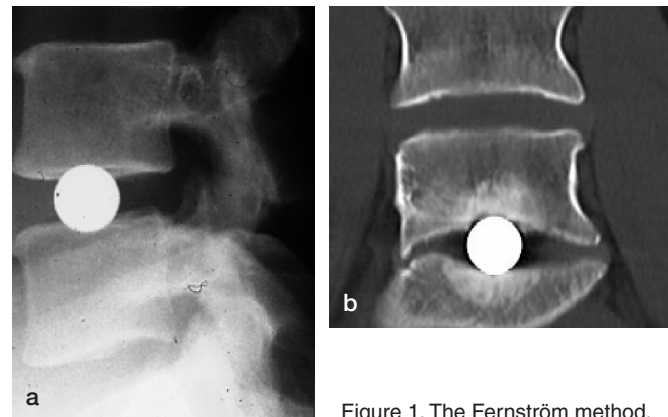


Figure 1. The Fernström method.

mobility in the painful segment. This could be beneficial while at the same time the segment is stabilised. The proposed "pain generator", the disc, is removed<sup>47</sup>. If surgery could maintain/restore near-physiological mobility the frequency of patients with ASD would possibly decrease<sup>34,79</sup>. Other features of a mobile solution have been proposed to be positive, such as "a more physiological solution" providing the patient with the possibility to find their own correct sagittal balance<sup>30,88</sup>.

TDR is performed with a disc prosthesis, that has two endplates (presently always metal) and between these an articulation where either metal articulates to polyethylene (as in many hip- and knee-prostheses) or there is a metal-to-metal articulation. The design of prostheses is either a "non-constrained" centre of mobility or a "semi-constrained" one. The non-constrained design features a mobile core that articulates with both endplates, thus the centre of rotation varies. The semi-constrained is more of a "ball and socket" design with a fixed centre of rotation.

Patients are mostly excluded from TDR if the posterior elements are not fairly intact (i.e. no spondylolysis) or if there has been removal of facet joints or severe arthritis appearing in these joints. Disc prostheses only restore the anterior part of the motion segment<sup>2,14,151</sup>. Patients with osteoporosis should not be considered for TDR, due to the risk of subsidence.

### Uncertainties with TDR

Several studies with long<sup>91,137</sup> or short-term results<sup>12,13,29,87,90,122,124,136,149</sup> compare TDR to fusion. Most of these report clinical outcome to be better or as good as fusion results. There are until now three randomised controlled trials (RCT) between TDR and fusion. All three claim a better result for TDR. These RCTs were performed to receive FDA (Federal Drug Administration) approval in the US. One was using the Charite' prosthesis<sup>14</sup>, one using the ProDisc prosthesis<sup>151</sup>, and one study briefly reporting on the Maverick prosthesis<sup>56</sup>. These studies are designed as "non-inferiority studies" with unequal randomisation (2:1) between TDR and ALIF.

Two-year results were recently presented (Hellum, Eurospine October 2009) from a RCT comparing TDR to conservative treatment according to modern principles, including CBT and “pain-school”. The results from the study were in favour of TDR.

The TDR procedure is today performed via an anterior approach in contrary to most lumbar fusions that are performed from posterior. Several studies report a high frequency of disturbances in sexual function, especially in men, after anterior lumbar surgery, mostly fusions<sup>18, 31, 43, 78, 113, 117, 133</sup>. The most frequent and severe complaint reported from these studies has been iatrogenic retrograde ejaculation. This has led to concern whether to use TDR in younger men, since it might cause sterility. The reports on a high frequency of this complication are connected to trans-peritoneal approach, laparoscopic or open, used in anterior fusion surgery. The complication seems to be technique-dependent<sup>82</sup>.

The effect on sex life in patients with non-specific neck or lumbar pain has been described in previous studies<sup>98, 110, 126</sup>. However the effect on sex life in the specific subgroup suffering from DDD has not been investigated.

The surgical goal of TDR is to maintain mobility of the segment. Long-term follow-up on predecessors to today's disc prostheses showed a low (40%) mobility<sup>112</sup>. This was explained by subsidence of the prosthesis into the endplates<sup>96</sup>. Commercially available designs today have far larger “foot-prints” i.e. endplates that transmit the pressure to the strong periphery of the bony endplate<sup>2</sup>. Long-term (8.7 years) follow-up of a modern prosthesis did not reveal deterioration in mobility with time<sup>62</sup>.

Accurate and reliable measurements of mobility in disc prostheses have been difficult to achieve<sup>95</sup> due to low accuracy<sup>94</sup>.

Precise and accurate measurement of segmental mobility pre- and postoperatively in treatment with TDR compared to treatment with fusion is now available using new technique<sup>51</sup>.

Previous reports indicate that there is less radiological deterioration at levels adjacent to a disc prosthesis if there is preservation of range of motion (ROM) in flexion-extension of more than five degrees as compared to less mobile implants<sup>34, 63</sup>. A recent study demonstrated differences in mobility at all levels in the entire lumbar spine between patients treated at one segment with TDR as compared to fusion<sup>6</sup>. It has also been

demonstrated that a segment treated with TDR has less mobility than a normal healthy segment. This is suspected to be an effect of preoperative soft tissue adaptation, perhaps in combination with fear of pain<sup>89</sup>, though that study did not include preoperative mobility measurements. Another study demonstrated a negative correlation between less mobile implants and outcome<sup>64</sup>.

Over the last decade the use of TDR has grown rapidly, even so, most of the above questions have not been answered<sup>47</sup>.

## Community perspective

Back problems, and especially LBP consume enormous resources in terms of health-care, sick leave and treatment<sup>80</sup>. In Sweden, as in many other European countries, the total health-care cost is reported to be approximately 8% of the gross national product, while in the US it has been reported to be the double<sup>108</sup>. Apart from the common cold, back pain with a lifetime incidence of about 80%, is the most common cause of seeking medical advice and being on sick leave.

LBP is also the cause of functional disability, suffering and reduction in life quality<sup>36, 84, 139</sup>.

A 69% life prevalence of LBP in Sweden<sup>59, 73</sup> and a recurrence rate as high as 86% have been reported<sup>141</sup>.

Due to the large impact of LBP upon the quality of life in many patients and upon the cost to society<sup>118, 119</sup>, we have strived for many decades to develop methods to diagnose and treat painful and disabling back problems. This has led to growth in our understanding of the complexity of back pain<sup>142</sup>, and “The Biopsychosocial Model” prevails as the best way to understand and treat LBP.

In today's health-care not only are clinical results in focus, but also the cost of achieving these results<sup>76, 77, 116, 127</sup>. A new method demands a thorough health-economic investigation to receive its correct place among the treatment options available for our patients. Until now only one rather limited, health-economy study has been published on treatment with TDR compared to fusion<sup>57</sup>.

It has been suggested that the TDR-procedure leads to shorter hospital stay and sick-leave compared to fusion, thus creating a saving for society<sup>14, 151</sup>.

## Aims of the thesis

The general aim of this thesis was to evaluate whether the new treatment option, TDR, is at any point beneficial or inferior compared to today's "gold standard" in the surgical treatment of DDD i.e. fusion. The specific questions were:

- I. What is the clinical outcome of TDR compared to fusion?
- II. Is there a difference in complication rate or severity of complications? Is there a difference in re-operation frequency?
- III. A) How does CLBP of assumed discogenic origin affect sex life and sexual function in terms of erection, orgasm and ejaculation in patients considered for surgery and are there differences in pain-related effects on sex life after treatment?  
B) Does sex life and sexual function improve when low back pain is relieved? Is there a difference in results on sex life and sexual functions and are there different adverse effects between the two methods?
- IV. A) How often are the primary surgical mechanical goals achieved, i.e. to create a stable fusion, or to restore/maintain mobility after TDR? Is there a significant correlation of clinical outcome between successful fusion or successful restoration of mobility after TDR?  
B) Is there a difference in disc height and alignment of treated segments between the groups? Is there any difference in mobility in adjacent segments between the two methods?
- V. A) Is there a difference in health-care costs, total costs for society or in length of sick leave postoperatively between the two treatments?  
B) How does the respective cost-effectiveness/utility compare when using the Quality-of-life instrument EQ-5D?

## Material

The present four articles are all derived from the same patient material. The patients were referred to the clinic for surgical evaluation. The Stockholm Spine Center provides health service to patients with degenerative disorders of the spine, based on contract with the County of Stockholm. Patients referred to the Stockholm Spine Center from Stockholm County are to a large extent sent by their GP or company physician. Sixty per cent of the patients in this material were referred from the County of Stockholm and this figure was the same for both treatment groups.

The remaining 40% of the patients were referred from other counties in Sweden, mostly from orthopaedic specialists in their home county who requested evaluation for surgery.

No self-paying or privately insured patients were part of this material.

### Inclusion and exclusion criteria

The patients in the current study had symptomatic degenerative disc disease in one or two motion segments between L3 and S1, with CLBP as a predominant symptom, although leg pain was not a contraindication. For inclusion in the study, back pain should be described as mechanical and supposedly discogenic in origin with inter-spinous tenderness and position dependent pain at examination. Disc narrowing on X-ray, and clear signs of disc degeneration on MRI were required. Low-grade facet joint arthritis at the index level, as well as low-grade degeneration at other levels, was accepted. Patients who fulfilled the inclusion criteria at the primary consultation but scored less on ODI and VAS at the time of surgery were included with their immediate preoperative values as baseline. The inclusion and exclusion criteria are summarised in Table 1. The exclusion criteria are those described by Huang et al.<sup>65</sup>, but modified to exclude patients that were not likely to be able to take part in a long-term study.

Among the patients referred to the clinic, 152 consecutive patients were included in the study after careful selection. To be selected for the study the patient was primarily judged to be a suitable candidate for surgery, according to the principles described above and secondly according to the inclusion and exclusion criteria of the study. To avoid bias, patients with a strong belief that one treatment option was superior to the other were not included. Forty-one patients (27%), underwent preoperative provocative discography and disc block, to identify pain-generating levels when there was clinical uncertainty as to whether to treat one or two segments.

**Table 1. Inclusion and exclusion criteria**

<p><b>Inclusion criteria</b></p> <ul style="list-style-type: none"> <li>• Low back pain (LBP) with or without leg pain for more than one year. If leg pain occurred, then LBP should dominate</li> <li>• Conservative treatment scheduled for more than three months had failed</li> <li>• Confirmation of disc degeneration on MRI</li> <li>• Age 20–55 years</li> <li>• Oswestry Disability Index over 30 or back pain (VAS) over 50/100 the week before inclusion</li> <li>• Signed informed consent</li> <li>• Open mind to the two treatment options</li> </ul> <p><b>Exclusion criteria</b></p> <ul style="list-style-type: none"> <li>• Spinal stenosis requiring decompression</li> <li>• Moderate or advanced facet joint arthritis.</li> <li>• Three or more painful levels at clinical examination</li> <li>• No obvious painful level, or levels, at diagnostic injection evaluation (if done)</li> <li>• Isthmic spondylolysis/olisthesis</li> <li>• Degenerative spondylolisthesis &gt;3mm</li> <li>• Major deformity</li> <li>• Manifest osteoporosis. If osteoporosis was suspected due to gender and age (females above 50), illness or medication, osteoporosis should be evaluated and excluded before inclusion</li> <li>• Previous lumbar fusion or decompression with postoperative instability (e.g. facet joint damage or wide laminectomy)</li> <li>• Compromised vertebral body</li> <li>• Previous spinal infection or tumour</li> <li>• Inability to understand information due to abuse, psychological or medical reasons</li> <li>• Language difficulties with inability to understand follow-up instruments</li> <li>• Pregnancy or other medical condition that would be a contraindication to surgery</li> </ul>
---

### Study population

In total 90 women and 62 men were included, with a mean age of 40 years (21–55 years).

After inclusion, patients were randomised between fusion and TDR by means of closed envelope technique. The planning staff drew the envelope when the surgeon's inclusion form and the patient's informed consent had reached the planning office via intra-hospital mail. The surgeons were not informed of the result of the randomisation until the patient arrived at the hospital for surgery: at which time the patients were also informed of the result of the randomisation.

*Baseline data:* There were no differences between the treatment groups concerning age, gender, smoking status, baseline Oswestry Disability Index (ODI), surgical levels, prior surgical treatment, or back pain and function. There was however a random statistically significant higher rating on leg pain VAS in the fusion group ( $p = 0.016$ ). Both treatment groups had the

**Table 2. Patient demographics:** The clinical scores as well as outcome measures are described below: Visual Analogue Scale (VAS), Euroqol (EQ5D), Oswestry Disability Index questionnaire (ODI), Low Back Pain (LBP). Mean values. Questions on sex life from question 8 of Oswestry Disability Questionnaire where two patients from each group did not answer

	TDR n=80	Fusion n=72	P	Total N=152
Female gender	48 (60%)	42 (58%)	0.715	90 (59%)
Age	40.2±8.1	38.5±7.8	0.229	39.4±8.0
Smokers	8 (10%)	8 (11%)	0.824	16 (11%)
Previous spinal surgery	10 (12%)	8 (11%)	0.792	18 (12%)
Back pain VAS	62.3±20.8	58.5±21.7	0.218	60.5±21.2
Leg pain VAS	32.8±26.4	43.7±28.2	0.016	37.9±27.7
EQ5D	0.42±0.31	0.36±0.33	0.167	0.39±0.32
ODI %	41.8±11.8	41.2±14.6	0.303	41.5±13.1
LBP >2 year	79%	87%	0.147	83%
One level surgery	45 (56%)	33 (46%)	0.200	78 (51%)
<b>Sex life:</b>				
Normal	11 (14%)	10 (14%)	0.975	21 (14%)
Normal but some pain	24 (31%)	27 (39%)	0.319	51 (34%)
Nearly normal, very painful	16 (21%)	14 (20%)	0.938	30 (20%)
Severely restricted by pain	23 (29%)	15 (21%)	0.263	38 (26%)
Nearly absent because of pain	2 (3%)	3 (4%)	0.562	5 (3%)
No sex life at all	2 (3%)	1 (1%)	0.625	3 (2%)

same proportion of “Stockholm County” patients and about 70% of the patients in both groups were on full sick-leave or medical retirement due to CLBP, thus 30% were working full- or part-time. All smokers were encouraged to give up smoking before treatment, but 16 patients still smoked during the study.

In all, 86% (127/152) of the patients reported disturbances in their sex life. The most frequent complaint (34%, 51/152) was that sex life was normal but caused some extra low back pain. 20% of the patients reported that sex life was normal but very painful. 31% of the patients reported their sex life as being severely restricted or prevented by low back pain (Table 2).



**Figure 2.** a) The Charité prosthesis implanted, from side and front, b) the Maverick prosthesis, and c) the ProDisc prosthesis

## Surgical groups

Eighty patients were treated with TDR and 72 with instrumented fusion.

The fusion technique was according to the attending surgeon's preference (PLF or PLIF) and consisted of instrumentation from a posterior approach. Thus, 44 patients had PLF and 28 PLIF.

In the TDR group the approach was anterior left extraperitoneal. Three different designs of disc prostheses were used (Figure 2).

The randomisation process was stratified for number of levels, one or two, to assure an equal proportion of one and two level patients with each prosthesis design.

## Methods

### General design

The study was a “single centre prospective randomised controlled trial (RCT) study”, performed at the Stockholm Spine Center.

### Data collection

Preoperative data as well as data on outcome at one and two years were registered in the Swedish Spine Register (SweSpine)<sup>131</sup>, a register that has been in use since the mid Nineties in Sweden and to which most clinics performing spine surgery report<sup>129</sup>. All questionnaires are sent to and registered at one location, and the clinics can acquire their results from this centre.

The register amongst other things contains the results from questionnaires that were filled out by the patients. Patients reported in these questionnaires if they were on sick-leave and if so, the reason for absence from it and their work status. They also reported on smoking habits and previous surgery. In addition patients filled out disease-specific function with ODI, Quality-of-life with EQ5D (EuroQol) and SF-36, VAS for back and leg pain separately and also at follow-up a question on patient satisfaction with treatment and a “Global assessment of (change in) back pain”.

The attending surgeon registered peroperative data on diagnosis, surgical procedure, levels, implants, bone transplantation and donor site, antibiotics, complications, and a possible reoperation. Medical records were checked for further complications, length of surgery and hospital stay, operation time and total blood loss.

Patients were given a special questionnaire, different for men and women, to study effects on sexual function. These were answered prior to treatment and at follow-up.

Lateral X-rays were taken in full extension and flexion preoperatively and at two-year follow-up for the radiological study on stability respective mobility.

To perform the health-economy study, data were gathered from Statistics Sweden (SCB. [www.scb.se](http://www.scb.se)), Stockholm Spine Center on health-care cost per patient (CPP), the Swedish Spine Register and from a “cost diary”<sup>55</sup>. Patients submitted the mailed cost diary to the study secretary; these data were used to assess utilisation of different services, after 1, 3, 6, 12, 18, and 24 months. All information about part-time or full-time sick-leave, as well as part-time or full-time work, was converted into full-day equivalents for purposes of analysis. Patients who failed to respond at any of the six specified follow-up periods were contacted by phone.

*Follow-up:* All patients had consultations at one and two years after surgery. They were questioned, physically examined and had X-rays, including flexion-extension films taken. We checked that the patients had sent in their questionnaires and cost diaries. All patients appeared at check-ups and also answered questionnaires from home at both one and two-year follow-up, resulting in a 100% follow-up rate.

### Clinical outcome measures

*Global assessment of back pain:* A self-reported descriptor of over-all result in a randomised trial of low back pain treatment<sup>68</sup>.

- 0: I had no back pain prior to the operation,
- 1: I have had total relief of back pain after the operation,
- 2: My back pain is much better after the operation,
- 3: My back pain is better after the operation,
- 4: My back pain is unchanged after the operation, and
- 5: My back pain is worse after the operation.

*Visual analogue score (VAS):* A ten-point scale on which patients’ are asked to score according to their level of back/leg pain (0=no pain and 10=worst pain imaginable)<sup>67,120</sup>.

*Oswestry Disability Index (ODI):* also known as The Oswestry Low Back Pain Disability Questionnaire<sup>44</sup>. This is a patient-reported outcome questionnaire comprising 10 items (subscales). Each subscale contains six statements. Each statement describes a greater degree of disability. Each subscale score is on a 0 to 5 point scale. The total score is doubled and expressed as a percentage. Minimum score is 0 and maximum 100. The higher the score, the greater is the disability. There are several modified versions where the sex life subscale (question 8) has been deleted or replaced by another item, but the original version is used in the Swedish Spine Register.

*SF-36:* A non-disease-specific self-reported questionnaire consisting of 36 questions evaluating health-related quality-of-life<sup>144,145</sup>. Results are presented as a profile in four physical domains (physical function, role physical, bodily pain, general health) and four mental domains (social function, role emotional, mental health and vitality).

*EQ-5D (EuroQoL):* A non-disease-specific self-reported questionnaire consisting of five questions that defines a total of 243 health states (from 1990)<sup>66,134</sup>. The five questions represent five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. There are three levels of severity: no problems, moderate problems and severe problems. The answers are converted into a number between zero and one, where best possible health state has the value one and death has the value zero, but negative scores are also possible

(worse than death). The results on this health-related quality-of-life questionnaire are usually used to calculate cost/benefit in health economy evaluation.

### **Clinical outcome and complication study**

Global assessment of back pain was the primary outcome parameter, and was compared between groups at one- and two-year follow-up, but also within groups to capture changes over time. Hägg et al. concluded "Patient global assessment is a valid and responsive descriptor of over all effect in randomised controlled trials of treatment for chronic low back pain"<sup>68</sup>.

The other outcome scores (VAS for back and leg pain, EQ5D, SF-36, ODI and patients satisfaction with the result of treatment) were compared to preoperative values as well as compared between groups at one and two years postoperatively.

ODI success was described as >25% improvement, compared to 15% in the FDA studies on TDR<sup>14, 151</sup>.

Complications and reoperations, including patients scheduled for reoperation, were recorded in the medical notes as they occurred and transferred onto our general data sheet. Grading into minor and major complications was done according to "The Swedish Spine Study"<sup>49</sup>.

### **Study on sex life and sexual function**

In this study focusing on sex life and sexual function, over-all "sex life" as associated with low back pain was determined using ODI question 8 that covers sex life. As with all 10 ODI items, this has a fixed relation to pain.

General Sex Life:

- 0p** – My sex life is normal and causes no extra pain,
- 1p** – My sex life is normal but causes some extra pain,
- 2p** – My sex life is nearly normal but is very painful,
- 3p** – My sex life is severely restricted by pain,
- 4p** – My sex life is nearly absent because of pain,
- 5p** – Pain prevents any sex life at all.

Sexual function, described as erection, orgasm and ejaculation in men and orgasm in women were investigated using separate questionnaires (see below), both preoperatively and after two years.

The questionnaire used to evaluate sexual function in "The Swedish Lumbar Spine Study"<sup>71</sup> was adapted also for preoperative use in this study. This meant that preoperatively current status of sexual function, not changes, was asked about. The preoperative questions regarding sexual function in men were used to evaluate erection and orgasm, and whether there was a problem with suspected retrograde ejaculation. As spine surgery can affect sensibility in the genital area, baseline information on this was collected before surgery. At follow-up, negative or positive changes in sexual function were identified. As several patients reported difficulty in understanding the question on retrograde ejaculation this question was complemented at follow-up or by telephone.

Changes in sex-life and sexual function were compared to clinical results on pain after treatment. Answers were given as Yes or No.

*Men: Pre-operative questionnaire on sexual function*

- M1.** Do you have any disturbance in your ability to have an erection?
- M2.** Do you have any disturbance in your ability to have an orgasm?
- M3.** Are you able to have an orgasm as normal, but without ejaculation?
- M4.** Do you have normal sensation in your genital area?
- M5.** Have you tried, but not succeeded in having children?
- M6.** Other comments

*Men: Questionnaire on sexual function at two-year follow-up*

- M1a.** Have you noticed any deterioration in your ability to have an erection after the operation?
- M1b.** Have you noticed any improvement in your ability to have an erection after the operation?
- M2a.** Have you noticed any deterioration in your ability to have an orgasm after the operation?
- M2b.** Have you noticed any improvement in your ability to have an orgasm after the operation?
- M3.** Have you noticed any change in that you can have an orgasm as normal, but without ejaculation?
- M4.** Have you noticed any change in sensation in your genital region after the operation?
- M5a.** Did you try, but not succeed in having children before the operation?
- M5b.** After the operation, have you tried, but not succeeded in having children?
- M6.** If you have answered "yes" to any question, please describe the changes that have taken place.

*Women: Pre-operative questionnaire on sexual function*

- W1.** Do you have any disturbance in your ability to have an orgasm?
- W2.** Do you have any disturbance of sensation in your genital area?
- W3.** Have you tried, but not succeeded in having children?
- W4.** Other comments?

*Women: Questionnaire on sexual function at two-year follow-up*

- W1a.** Have you noticed any deterioration in your ability to have an orgasm after the operation?
- W1b.** Have you noticed any improvement in your ability to have an orgasm after the operation?
- W2.** Have you noticed any changes in sensation in your genital area after the operation?
- W3a.** Did you try, but not succeed in having children before the operation?
- W3b.** After the operation, have you tried, but not succeeded in having children?
- W4.** Have you noticed any other changes in your genital area?
- W5.** If you have answered "yes" to any question, please describe the changes that have taken place?

Table 3. Definition of parameters determined by DCRA, valid for segments Th12/L1 to L5/S1 (see also figure 1)

DCRA parameter	Definition, c.f. Figure 3
<b>Mean vertebral depth</b>	Mean of distances of corners 1 and 2 and corners 3 and 4.
<b>Sagittal plane angle</b>	Angle between vertebral midplanes. The vertebral midplane is defined as the line running through midpoints between corners 1 and 3 and 2 and 4 respectively.
<b>Disc height</b>	Sum of distances of corners 2 and 4 from the bisectrix between the midplanes, divided by the mean depth of the cranial vertebra. Disc height as defined here is a logical further development of Farfan's definition. Disc height can be compared with age- and gender-appropriate normal data. As the given sagittal plane angle will usually differ from the reference angle of the normative database, a correction is applied prior to the comparison. The correction depends linearly on the difference between the given sagittal plane angle and the appertaining reference angle of the norm. The deviation of the corrected disc height, or (in the case of TDR) of the corrected height of the intervertebral space from the norm is then independent of the sagittal plane angle adopted when the radiograph was taken. In this study, the term 'disc height' is used synonymously with 'intervertebral space'.
<b>Postero-anterior (dorso-ventral) displacement</b>	Distance between the projections of the centre points (geometric centres of corners 1 to 4) of the vertebrae onto the bisectrix, divided by the mean depth of the cranial vertebra. Displacement is counted positive, if the cranial vertebra is displaced in anterior direction with respect to the caudal vertebra. Displacement can be compared with age- and gender-appropriate normal data. As the given sagittal plane angle will usually differ from the reference angle of the normative database, a correction is applied prior to the comparison. The correction depends linearly on the difference between the given sagittal plane angle and the appertaining reference angle of the norm. The deviation of the corrected displacement from the norm is then independent of the sagittal plane angle adopted when the radiograph was taken. This holds for mobile as well as for fused segments.

### Study on mobility, disc height and translation in operated and adjacent levels

In this study digital radiographs were acquired preoperatively, postoperatively and at the one- and two-year follow-ups. The radiographic examination was performed in supine position and consisted of a standardised AP-view and lateral views in flexion and extension. Measurements were achieved with a new digitalised method, Distortion Compensated Roentgen Analysis (DCRA) that allows for a measuring error of one degree and one millimeter. The DCRA protocol<sup>51</sup> permits measurements from all segments on a lateral view and compensates for image distortion caused by axial rotation, lateral tilt and off-centre positioning of the spine. This allows also for calculation of changes in disc-height, sagittal alignment, translation and mobility at segments treated with either TDR or fusion. The same measurements were performed in segments adjacent to the ones treated. Table 3 summarises the definition of the parameters measured by DCRA and Figure 3 illustrates these definitions.

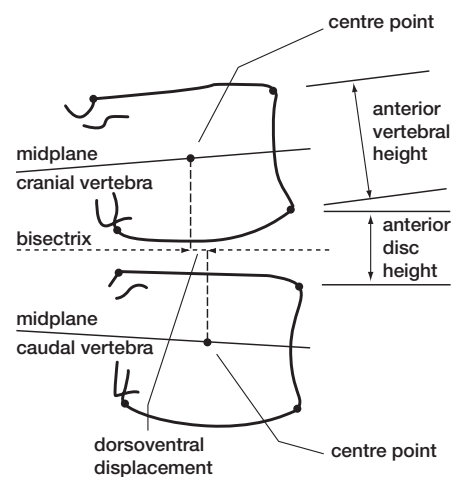


Figure 3. Parameters determined by distortion-compensated roentgen analyses (DCRA). Example of the contours of a lumbar motion segment imaged off-centre and slightly rotated. Corners 1-4 are objectively located by computer programme. Raw values of disc height and posterior-anterior displacement are derived from the relative location of the corners.

This allows for an accurate conclusion on whether the disc prosthesis moves after two years, and if so, how much. In fusion cases we were also able to determine the success of immobility of the treated segment. It was then possible to calculate how successful we were in achieving the primary surgical goal, mobility respective immobility.

### Health economy study

From data collected at four sources (Statistics Sweden, Stockholm Spine Center, Swedish Spine Register and "cost diary"), hospital costs and total costs were calculated for each patient, and the two groups were compared. By adding the information from the EQ5D (EuroQol) it was possible to make calculations on cost-effectiveness/utility, including cost/QUALY (cost per gained step in life quality) and net benefit.

### Statistical analysis

#### Clinical outcome and complication study

**Power estimation:** The "Clinical outcome study" was dimensioned to compare TDR and fusion with global assessment of back pain at two years as the primary outcome variable. "Total relief" was considered as the optimum result and primary endpoint, whereas "much better" was interpreted as essential improvement in contrast to "better", "unchanged" and "worse". The Lehr formula was used to provide crude estimates of sample size. With 80% power at 5% significance level, the size of each group was estimated at 64 patients, which was increased to 72 to allow for potential dropout.

Results are given as means, standard deviations and ranges. For comparison between the treatment groups, and for some

subgroup analyses, two-tailed Mann-Whitney U-test and Wilcoxon rank sum tests were used. For ordinal data, Student's t-test was used, and for categorical data, e.g. global assessment, Spearman R, Fisher's exact and Chi-square tests were used. Multivariate statistics were used to analyse predictors. Statistical significance was defined as  $P < 0.05$ .

#### **Study on sex life and sexual function**

Categorical data were tested with Fisher's exact test or the Chi-Square-test and continuous data with the Mann-Whitney U-test. Multiple regression analyses were performed separately for men and women and for those who underwent each surgical technique. Differences between groups were tested using non-parametric tests (Mann-Whitney U-test and Chi-Square). Correlations were calculated with Spearman rank R.

#### **Study on mobility, disc height and translation in operated and adjacent levels**

The disc height and displacement are not given by their absolute values but by their deviation from the gender-, age- and level-appropriate normal values<sup>51</sup>. Deviation is measured in units of the SD (standard deviation) of the norm. For example, a value of  $-1.0$  denotes that the respective parameter assumes a value of 1 SD below the norm. Characterising measured data by their deviation from the norm or predicted in units of the standard deviation allows disc height and displacement data from different levels to be pooled.

For comparison of disc height and vertebral alignment with the normative database, the difference in standard deviation (SD) from gender-, age- and level-appropriate normative values preoperatively was computed against the deviation from pre- and two years postoperatively. For comparison of range of motion (ROM) the actual measured degrees are reported and computed. Student t-test, Fishers exact test,

Mann-Witney-U and Pearson Product Moment Correlation as well as Spearman rank correlation were used. Level of significance was set at  $P \leq 0.05$ .

#### **Health economy study**

We used the results presented in the Swedish Lumbar Spine Study<sup>50</sup>. Standard deviation (SD) was estimated from that study at SEK 250,000 (EUR 26,998, USD 33,875). To achieve 80% power and a 5% level of significance, a total of 64 patients were required in each group. It was decided to expand the study groups to 72 patients each to allow for potential dropout. Since improvement and return to work rate are dichotomous variables, we used the McNemar exact test; for continuous variables, we used the Wilcoxon signed test. For testing differences between the two groups regarding costs and other non-normal clinical variables, we used the Mann-Whitney U test. All baseline data were compared between the study groups using a significance level of 0.05. To analyse confidence intervals for cost and effect differences and for ratios we used the bootstrapping technique (resampling 10,000 times).

Statistical analysis was made using the SPSS statistics programme (version 17.0) for the health economy study, all other statistics were performed using Statistica version 7 (StatSoft Inc. Tulsa, OK, USA).

#### **Ethical considerations**

All studies were conducted in conformity with the Helsinki Declaration.

The study design in all its parts and protocols were approved by the Ethics Committee of the Karolinska Institute, Stockholm in 2003 (03-268).

All patients provided written informed consent before participation.

## Results

*Follow-up:* This study had 100% follow-up at both one- and two-years on visits and on returning questionnaires on clinical outcome. The response for preoperative ODI 8 and questionnaires on sexual function was 97% (148/152). The X-ray measurements were performed on the entire material except four patients where the preoperative x-rays were missing.

Follow-up of cost diaries was 100% at 1, 3, and 6 months, 95% after 12 months, 96% at 18 months, and 99% at 24 months.

### Clinical outcome and complication study

Data from the hospital stay at the index operation are shown in Table 4.

Length of hospital stay and time of surgery were shorter in the TDR group compared to the fusion group.

There was no difference in intra-operative blood loss between groups.

Outcome variables improved in both groups at the follow-up as compared to preoperative values (Table 5). 35/152 of the patients in the current study reported total freedom of pain at the two-years follow-up, while an additional 67/152 of the patients reported being “much better”. In total 67% had a very good result from the surgical intervention. The average reduction in back pain VAS was 33.3 for the whole material, while the mean EQ5D improvement was from 0.39 to 0.68. The mean ODI score prior to treatment was 41.5, while their postoperative ODI was reduced to 21.4 at two-year follow-up.

The primary outcome measure, Global Assessment of back pain, revealed that 30% in the TDR group and 15% in the fusion group were totally pain-free at two years ( $p=0.031$ ).

The TDR group had less back pain (VAS) at two years ( $p=0.048$ ) than the fusion group.

Table 4. Intra-operative data and length of hospital stay. P-value of difference between TDR and Fusion

	Total N=152	TDR n=80	Fusion n=72	P-value
Intra-operative blood loss (mL)	505±335	560±400	444±228	0.185
Operating time (hours)	2.5±0.7	2.3±0.8	2.7±0.6	<0.001
Length of hospital stay (days)	5.1±1.6	4.4±1.6	5.9±1.2	0.000
Length of hospital stay after index episode	4.6±4.3	1.8±1.5	7.7±6.2	0.000

Table 5. Outcome: “Global assessment of pain” and other parameters

	Preoperative			1 year			2 years		
	TDR	Fusion	P-value <sup>a</sup>	TDR	Fusion	P-value <sup>a</sup>	TDR	Fusion	P-value <sup>a</sup>
Totally pain-free	–	–	–	23 (29%)	7 (10%)	0.003	24 (30%)	11 (15%)	0.031
Much better	–	–	–	35 (44%)	38 (53%)	ns	32 (40%)	35 (49%)	ns
Better	–	–	–	12 (15%)	15 (21%)	ns	14 (18%)	16 (22%)	ns
Unchanged	–	–	–	7 (9%)	7 (10%)	ns	5 (6%)	7 (10%)	ns
Worse	–	–	–	3 (4%)	5 (7%)	ns	5 (6%)	3 (4%)	ns
VAS back pain	62.3±20.8	58.5±21.7	0.218	25.5±26.5	33.4±26.8	0.030	25.4±29.8	29.2±24.6	0.048
Difference pre-postop	–	–	–	36.8±30.0	25.1±34.2	0.027	36.9±31.0	29.3±31.6	ns
VAS leg pain	32.8±26.4	43.7±28.2	0.016	13.2±21.9	20.6±25.1	0.007	16.4±24.5	20.7±24.3	0.037
Difference pre-postop	–	–	–	19.6±32.1	23.1±32.7	ns	21.0±26.4	23.2±28.1	ns
EQ5D	0.42±0.31	0.36±0.33	0.167	0.71±0.28	0.63±0.27	0.046	0.67±0.33	0.69±0.25	ns
Difference pre-postop	–	–	–	0.25±0.36	0.33±0.38	0.057	0.25±0.36	0.33±0.38	ns
ODI %	41.8±11.8	41.2±14.6	0.303	19.5±18.7	24.9±16.1	0.023	20.0±19.6	23.0±17.0	ns
Difference pre-postop	–	–	–	22.4±17.8	16.3±18.4	0.036	21.9±18.9	0.33±0.38	ns
ODI success	–	–	–	49%	44%	ns	39%	31%	ns

<sup>a</sup> P-value between groups

**Table 6. Complications and reoperations.** The complications documented in both groups were equal, in the fusion group (21%) and in the TDR group (18%,  $P=0.747$ ). There were more performed or planned reoperations in the fusion group at two-year follow-up (35%) than TDR group (10%,  $P=0.0002$ ) over the study period. The types of operations are listed

	TDR n=80	Fusion n=72	Total N=152
No complication	66	57	103
Infection	0	4 <sup>a</sup>	4
Haematoma	2	1	3
Facet joint problem	6	0	6
Pseudarthrosis	0	2 <sup>a</sup>	2
Wound hernia	1	0	1
Nerve entrapment	1 <sup>a</sup>	0	1
Donor site pain	0	1	1
Adjacent	1	6	7
Dural tear	1	1	2
Meralgia paresthetica	1	0	1
Subsidence /re-operation	1 <sup>a</sup>	0	1
Total complication	14	15	48
No reoperation	72	45	117
Extraction of pedicular screws	0	20	20
Decompression	1	0	1
Extraction of pedicular screws together with decompression	0	1	1
Fusion at TDR level	4	0	4
TDR above fusion	0	5	5
Haematoma removal	2	0	2
Hernia repair	1	0	1
Repair of dural tear	0	1	1
Total reoperations	8	27	35

<sup>a</sup> Major complications

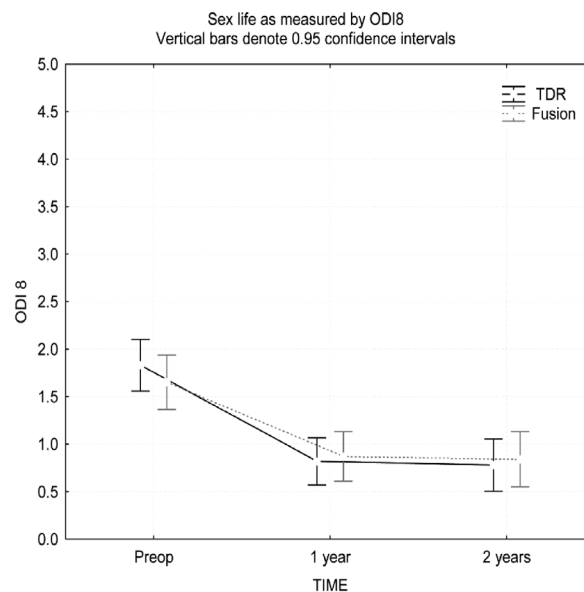
In virtually all other variables, TDR patients reached maximum recovery at one year, with significantly better results than the fusion group; whereas, the fusion patients continued to improve, reaching the same stage in outcome measures as TDR patients at two-year follow-up, except for Global Assessment of back pain and back pain VAS.

The TDR group had less leg pain (VAS) after two years, but that was already the case at randomisation. There was no difference in outcome between one or two-level surgery, or between different TDR devices, nor the two different fusion techniques (PLF and PLIF).

Complications were of equal number between the groups, in the TDR group one was classified as major compared to six in the fusion group<sup>49</sup> (Table 6).

Twenty patients in the fusion group with recurrent low back pain and complaints of tenderness over the instrumentation were offered reoperation with implant removal, of these seventeen were actually performed. Apart from these reoperations, the reoperation frequency was equal in both groups.

There were no complications with assumed association with design or materials in the disc prostheses.



**Figure 4.** Overall sexual life as reported on ODI8 pre- and postoperatively. There was a significant positive difference between patients before and after surgery, but no difference between treatment groups. ODI8: See page 13.

**Table 7.** Change in ODI8 postoperatively. In all 13/152 patients reported a deterioration of their sex life postoperatively, while 85/152 reported improvement and 47/152 were unchanged

		Improved					Deteriorated		
		-5	-4	-3	-2	-1	0	1	2
TDR	F	0	1	7	11	8	15	2	
	M	1	0	3	8	7	8	3	0
Fusion	F	0	2	3	5	11	17	1	0
	M	0	0	2	3	14	7	1	3
Total		1	3	15	27	40	47	7	6

### Study on sex life and sexual function

The majority of patients had impaired sex life because of low back pain before surgery. After surgery, sex life improved in both groups, with a strong correlation to reduction in low back pain. There was no significant difference in sex life reported by ODI8 between the groups neither preoperatively ( $p=0.401$ ) nor postoperatively ( $p=0.302$ ) and no differences between men and women preoperatively ( $p=0.094$ ) or postoperatively ( $p=0.308$ ) (Figure 4).

At two-year follow-up, sex-life according to ODI 8 had improved in both groups ( $p<0.001$ , Table 7). The improvement correlated with most clinical outcome measures, the strongest correlation ( $r$ ) being with back pain (preoperatively  $r=0.34$  and postoperatively  $r=0.71$ ) and with the entire ODI (preoperatively  $r=0.53$  and postoperatively  $r=0.71$ )

Table 8. Pre- and postoperative mobility in segments treated with either TDR or fusion, mean and (SD)

Segment	Mobility All patients preop.	Mobility TDR postop.	Mobility Fusion postop.	P-value <sup>a</sup>	P-value <sup>b</sup>	Mobile fusions	Immobile TDR
L3–L4	3.9° (4.0°)	8.0° (2.5°)	1.2° (1.1°)	<0.002	<0.001	0	0
L4–L5	7.3° (4.3°)	10.3° (4.8°)	1.3° (2.9°)	<0.005	0.0000	11 (27%)	3 (8%)
L5–S1	6.0° (5.0°)	9.0° (4.7°)	0.7° (2.5°)	<0.002	0.0000	5 (11%)	8 (15%)

<sup>a</sup> Significance of difference in mobility preop./postop. for TDR.

<sup>b</sup> Significance of difference in mobility postoperatively between TDR and Fusion.

Improvement in sex life correlated with both a decrease in back pain VAS ( $r=0.55$ ,  $p<0.001$ ) and an improvement regarding “global assessment of back pain” ( $r=0.55$ ,  $p=0.000$ ).

**Men:** The gender-specific questionnaire on sexual function revealed no negative effect of TDR in men (41% (62/152) in the study population).

**Erection:** Disturbance prior to surgery was reported by 11% (3/27) in the fusion group. After two years five (19%) of the fused patients reported deterioration and one (4%) an improvement. There was no difference correlated to fusion technique. In the TDR group 17% (5/30) reported an erection disturbance preoperatively. At two-year follow-up two patients (7%) reported deterioration compared with preoperative status, and five (17%) an improvement.

**Orgasm:** Disturbance was reported by 7% (4/57) preoperatively, and two-years after surgery more men in the fusion group (7/27), than in the TDR group (1/29), reported a deterioration in their ability to have an orgasm ( $p=0.023$ ), Difference in proportion: 26%–3% = 23%, CI: 5%–40%. The differences were not correlated to fusion technique, pain or any other variable.

**Retrograde ejaculation:** 6% (3/50) reported normal orgasm but without ejaculation preoperatively. These three patients reported normal ejaculation after their operation. Postoperatively 7% (4/56) reported suspected retrograde ejaculation, three after TDR and one after a PLF. Within their group, these patients reported less than average postoperative back pain, and proportion-wise had the same ODI8 result as for the whole group. The impairment resolved spontaneously within one to two months.

**Women:** Women comprised 59% (90/152) of the study population. At the time of surgery, impaired orgasm was reported by 23% (19/82). Postoperatively, there was no difference between the number of women reporting improvement and those reporting deterioration between groups. There was no difference in ability to have an orgasm between the two surgical groups postoperatively or between the fusion techniques.

For both men and women, improvement in sexual function correlated to improvement in back pain postoperatively ( $r=-0.57$ ), but also to improvement in leg pain ( $r=-0.33$ ), EQVAS ( $r=-0.45$ ) and EQ5D ( $r=-0.51$ ). The questions on sensation in the genital area and on being unsuccessful in having children postoperatively revealed no differences between gender and type of surgery.

## Study on mobility, disc height and translation in operated and adjacent levels

### Results according to the surgical goals

**Fusion group:** At the two-year follow-up the fused segments in general still exhibited some sagittal plane rotational motion. Sixteen patients developed a pseudarthrosis (22%), of which twelve had been treated at two segments. The pseudarthrosis-rate is shown in Table 8.

**TDR group:** There was a marked difference in mobility at treated segments between fusion and TDR (Table 8). The ROM of segments instrumented with TDR increased compared to the pre-treatment ROM, but remained lower than segmental ROM of healthy subjects. The increase in ROM was particularly seen in the extension domain, where most reduction was also seen preoperatively. Segmental fusion was observed in 11 of a total of 113 (9.7%) segments instrumented with TDR and in nine of 80 treated patients (11.2%). Three of the fused TDR's occurred in patients treated at two levels, with mobility in the other prosthesis, and in two patients there was fusion at both levels treated.

**Adjacent segments:** ROM and translation increased in the adjacent segments in both treatment groups. The increase was somewhat larger in the fusion group, but still within the normative range.

When L4–L5 was the adjacent segment, dorso-ventral displacement was larger in the fusion group ( $p<0.009$ ).

**Disc height:** In both fusion and TDR groups, disc height of segments selected for surgery was between 1 and 2 SD lower than in the normative database. After fusion, disc height was still lower than normal, whereas after TDR disc height was approx. 2–3 SD above normal. Disc height of the untreated segments both in fusion and TDR groups did not change compared to preoperative values.

No significant correlations were found between preoperative disc height and postoperative ROM or between postoperative disc height and ROM in the TDR group.

**Correlation between clinical outcomes as documented in SweSpine, and the results of fusion or TDR:** Sixty-four per cent of patients in the fusion group reported being pain-free or much better.<sup>68</sup> Fusion was achieved in 78%. There was no difference in clinical outcome (back pain VAS at two years) between solid fusions or patients with pseudoarthrosis.

Table 9. Mean cost/patient in the TDR and Fusion group two years following treatment

	TDR (n=80)		Fusion (n=72)		Diff <sup>a</sup>	95% CI Bootstrapping
	mean	SD	mean	SD		
1. Hospital costs index procedure (cost per patient)	105,613	25,688	107,111	15,589	-1,498	(-8,093 to 5,338)
2. Hospital costs after index procedure <sup>b</sup>	15,502	24,074	33,347	42,353	-17,845	(-29,111 to -7,078) <sup>b</sup>
3. Total hospital costs (1+2) <sup>b</sup>	121,115	36,897	140,458	42,253	-19,343	(-32,355 to -6,747) <sup>b</sup>
4. Primary/Private Care	24,146	64,793	26,726	28,597	-2,580	(-16,167 to 14,795)
5. Back-related drugs	2,489	3,461	3,562	4,819	-1,073	(-2,458 to 238)
6. Healthcare perspective (direct costs) (3+4+5) <sup>b</sup>	147,750	73,408	170,746	58,290	-22,996	(-43,055 to -1,202) <sup>b</sup>
7. Family support, housekeeping	12,879	16,114	16,685	21,444	-3,806	(-10,213 to 2,095)
8. Productivity loss (indirect costs)	438,931	371,542	498,488	389,313	-59,557	(-179,503 to 62,816)
9. Societal perspective (direct+indirect costs) (6+7+8)	599,560	400,272	685,919	422,903	-86,359	(-214,332 to 45,605)

<sup>a</sup> Minus in the Diff column means that fusion was more costly, however not significantly so with exception for <sup>b</sup> below  
<sup>b</sup> Hospital costs and also Health care costs differed significantly between groups due to more reoperations (mostly removal of implants) in the Fusion group.

In the TDR group 70% reported that they were “pain free” or “much better”. Preserved or restored mobility was achieved in 89%, though no correlation to clinical outcome (back pain VAS at two years) was found.

Motion at adjacent segments did not correlate to outcome.

### Health economy study

At baseline 30% in both groups were working part- or full-time.

After less than three months 30% of the total TDR group (24/80) and 18% of the total fusion group (13/72) had returned to work ( $p=0.102$ ). After one year 71% of the TDR group and 68% of the fusion group were back at work (full or part-time:  $p=0.776$ ). At two years, 76% of the TDR group and 72% of the fusion group were back at work (full or part-time:  $p=0.750$ ).

The number of full days sick-leave (with SD) following the index episode in the TDR group and the fusion group among those returning to work full- or part-time was 185 (146) and 252 (189) respectively ( $p=0.129$ ). Number of sick-leave days among those who returned to full-time work in the two groups was 139 (108) and 166 (132) respectively ( $p=0.740$ ), while sick leave days among those returning to part-time work was 336 (159) and 419 (173) respectively ( $p=0.211$ ).

The mean health-care cost/patient for TDR was SEK 147,750 (SD 73,408) and in the fusion group SEK 170,746 (SD 58,290). The difference expressed as TDR minus fusion was 16% and significant: -22,995 (CI: -1,202 to -43,055).

The mean cost/patient to society in the TDR group was SEK 599,560 (SD 400,272) and in the fusion group SEK 685,919 (SD 422,903). The difference of 14% was not significant: -86,359 (CI: 45,605 to -214,332).

The costs showed a wide spread, and despite the seemingly large differences in absolute costs, this made most of the differences non-significant (Table 9).

Quality-of-life (QoL) significantly improved in both surgical groups when comparing preoperative status with the situation at one and two years, TDR showing 0.41 EQ-5D units

and fusion showing 0.40 EQ-5D units, which translates to a non-significant QALY (quality adjusted life-years) gain of 0.01 units in favour of the TDR group over two years.

### Cost-effectiveness and net benefit

Incremental cost-effectiveness ratio (ICER) for EQ-5D using TDR instead of instrumented fusion was SEK 1,863,590. Statistic analysis detected that TDR was less costly and slightly better with regard to improvement in quality-of-life. Due to spread and variance, these conclusions are uncertain (Figure 5).

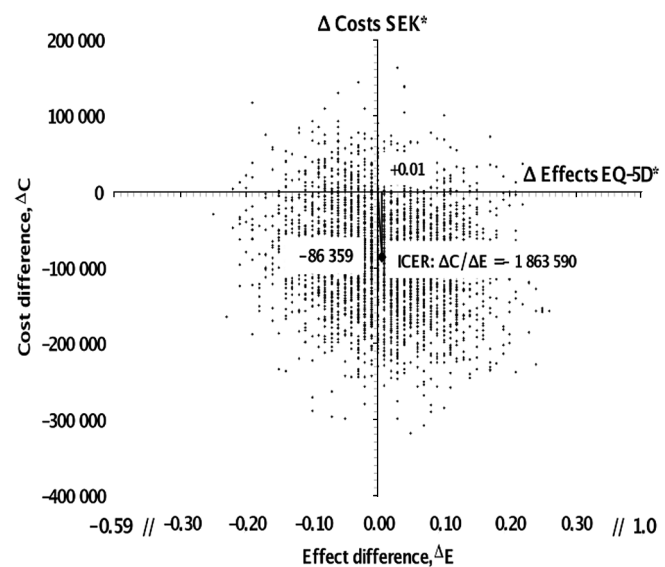


Figure 5. Cost-effectiveness plane illustrating ICER for TDR compared with FUS. ICER is located in the south-east quadrant, indicating that TDR was less costly and slightly more effective. However not significantly so. \* Difference ( $\Delta$ ) in costs and effects between TDR and FUS. Minus in costs and plus in effects favors TDR. Statistics: Bootstrapping was used. The dotted area represents the uncertainty (“uncertainty box”), with representations in all four quadrants, illustrating the uncertainty in the calculations.

The mean ICER was located in the southeast quadrant, indicating that TDR was cost-saving (i.e. less costly) and associated with a small improvement in QoL, albeit not significant compared to fusion.

The non-significant net benefit using TDR instead of fusion was in favour of TDR (SEK 91,359) after two years.

## Discussion

Questions on the diagnosis itself (CLBP) are unsolved, but so are questions on which patients to include in this diagnosis group.

Which patients with CLBP due to DDD are likely to gain from surgery<sup>28</sup>? It is difficult to find criteria for patient selection in the literature (menu and/or algorithms), and this has been pointed out as an area for future research<sup>3</sup>. It is obvious that a number of patients with LBP due to DDD, with long-lasting problems and significant disability, achieve good results from fusion as well as TDR surgery, but far from all. Patient selection seems to be crucial<sup>35</sup>.

Mannion et al.<sup>103,104</sup> found the following negative predictors for satisfactory results from spine surgery: Long duration of symptoms, severity of pathology on MRI (for disc herniation only), comorbidity, other joint problems, poor general health, psychological distress (e.g. depression, anxiety) especially in patients with chronic pain, family reinforcement of pain (especially in patients with chronic pain), smoking (especially for fusion), job dissatisfaction/resignation, employment compensation, long-term sick-leave/work disability. “Not working” was the major factor associated with a negative result after fusion surgery for spondylolisthesis found by Ekman et al.<sup>41</sup>. Hägg et al.<sup>70</sup> confirmed earlier reports<sup>121</sup> that low preoperative disc height was a positive predictor of satisfactory result in fusion, while long sick-leave before intervention was a negative predictor both for conservative treatment and fusion surgery.

Discography may add information on painful discs but is not to be overestimated as a diagnostic tool since the method has both false negative and positive results<sup>22,102</sup>. Recently, late results after discography have shown iatrogenic degeneration in discs examined<sup>23</sup>. In the current study discography was only used when uncertainty was felt on whether to treat one or two levels.

The three published RCT's in this field compare TDR to fusion, with results in favour of TDR<sup>14,56,151</sup>. These trials were designed to fulfil the needs for achieving approval by the FDA in the US. It seems that the inclusion and exclusion criteria were even stricter than in this study, and randomisation was 2:1. The studies were designed as “non-inferiority” studies. It might be questionable to draw conclusions on superiority from a study designed to prove non-inferiority<sup>17</sup>. When presenting the results from these studies, non-randomised trial cases were included in the statistics of the outcome, leading to difficulty in interpreting the results, and the results have been questioned.

The current studies were RCT's with 1:1 randomisation. We have compared the results from the clinical outcome study

to the results of an age-matched cohort of patients that were not randomised and that have undergone the same two treatments at our clinic<sup>11</sup>. This comparison revealed that the non-randomised cohort had differences at baseline between the patients that received TDR respective fusion. The differences in outcome were also larger in favour of TDR when there was an active choice of treatment option. Non-responders to postoperative questionnaires in the non-randomised cohort were not representative. In the current RCT we had no non-responders to postoperative questionnaires.

Patients in both treatment groups in the current study had an obvious improvement after treatment, well comparable with satisfaction after total hip replacement<sup>132</sup>.

TDR group had better results in several clinical outcome parameters at one-year follow-up. The results were similarly positive after two years. The fusion group had less improvement between baseline and one-year follow-up but had improved by the two-year follow-up, which explains why many significant differences that were present at one-year follow-up were lost (some barely) at the two-year follow-up. GA, the main outcome score as well as “VAS back pain” remained better in the TDR group even after two years. These findings, together with data on sick-leave postoperatively might lead to the conclusion that the time from treatment to improvement is shorter when TDR is used compared to fusion.

The results for the fusion group in our study, albeit inferior to the results in the TDR group, were dramatically better compared to what we achieved in “The Swedish Spine Study”<sup>48</sup> in the mid-nineties. In that RCT only 29% of the fused patient reported themselves to be pain-free or much better, compared to 64% in the current study. The reasons for this substantial improvement in outcome of fusion in only ten years are unclear. More sophisticated surgical techniques, improved implants and uniform (single centre) patient selection in the current study are possible reasons.

Despite the over-all good results, however approximately 30% of our subjects had an outcome that can be considered sub-optimal (better, unchanged and worse). What is the cause of this relative failure?

1. Did the operation fail in the sense that it was technically unsuccessful? We could not demonstrate any technical problems predicting bad outcome.
2. Did the operation fail in the sense that the surgical goal was not achieved? We were not able to demonstrate that fusion patients with residual movement (pseudoarthrosis) or prosthesis patients with loss of mobility (fusion) had worse outcomes.
3. Could the adjacent segments be adversely affected by the

operation? This was not supported by the x-ray results at two-year follow-up.

4. Had we operated on the wrong level/levels in failure cases?
5. Did we actually operate on some patients who were not suffering from CLBP due to DDD? There might have been other sources of pain or another type of pain syndrome.

The patients with a less favourable result on TDR or fusion in the current study (reporting: better, unchanged and worse) are possibly closely related, since the improvement in the “better” group was ten to fifteen points on the 100-graded VAS-scale, in the “unchanged group” was about five points better and in the “worse” group was between five points better to ten points worse than their rating at baseline. Hägg et al. previously calculated the minimal clinically important difference (MCID) of VAS back pain to be 18–19 points, well exceeding the 95% tolerance interval, which was 15 points<sup>69</sup>. As compared to the group reporting “totally pain-free” that on average rated their VAS at 2/100 implying a reduction in pain by approximately 60 points. The corresponding figure for the “much better” group was 10/100 and a gain of approximately 50 points.

There are some expected types of bias when using GA<sup>68</sup>. Recall bias might influence answers, but with this RCT study one would expect this to be even between the groups. Another type of bias that might have affected GA answers is the potential motivational bias, which implies that placebo effect of surgery might bias the patient’s answers. In this study all patients were operated on with surgery of similar magnitude. When TDR, the “new” treatment took place (2003–2005), this technique was not generally known to the public in Sweden. Patients who had a strong opinion on any of the methods compared in these studies were not enrolled. If a patient preferred a fusion, he or she was just planned for that as normal, and had their fusion in due course. If a patient preferred TDR, he or she was informed that at time we did not do disc prosthesis surgery outside the study, but was welcomed back later. During the time of enrolment to the study, only a few patients referred for surgical evaluation of pain due to DDD demanded specific treatment with either TDR or fusion, and thus were not enrolled.

A possible explanation for the difference in results between the two groups, not being dependent on the aim of treatment (mobile or stable), could be the difference in surgical trauma that comes with the respective surgical method. Datta et al.<sup>32</sup> reported that patients having longer exposure to muscle retraction during spine surgery performed via a posterior approach had more low back pain compared to patients with shorter muscle retraction. This difference was still present six months after surgery. Weber et al. on the other hand recognised muscular changes postoperatively after posterior lumbar surgery but found no correlation to pain<sup>147</sup>. Considering the time to follow-up it is unclear how much the time of retraction of posterior muscles affects clinical outcome after two years. However this specific factor could certainly have influenced the

figures on return to work within the first few months after surgery. The surprising result regarding men in the fusion group reporting deterioration in ability to have an orgasm might be related to postoperative changes in the lumbar musculature.

A possible factor in favour of the fusion group is that fusion directly treats pain related to the facet joints, while TDR does not. So, if pain originates from the facet joints, fusion should give a better result. On the other hand primary pain from the facet joints is nowadays considered a rare condition<sup>10,15</sup>. Secondary pain from the facet joints could possibly arise after TDR, especially if the segment altered its ROM towards the extension domain, as was the case in the L5–S1 segment in the current study<sup>138</sup>.

At this point it is not possible to have an opinion on whether or not one disc prosthesis design is better than the other, and over the last few years several new designs have been introduced. New MRI-compatible prosthesis materials are being developed. Experiences gained from The Swedish Hip Register<sup>132</sup> on survival of different designs make it interesting to follow new TDR designs over a long time-span.

We found no difference in outcome or complications whether one or two segments were treated, and we could not confirm the concerns of Ching et al.<sup>26</sup> regarding symptomatic coronal plane deformity after two-level arthroplasty.

Complications were equal between the two groups. Reoperation frequency was similar between the groups, except for a high number of fusion patients who had their instrumentation removed. This was offered to patients with recurrent back pain and tenderness over the heads of the pedicle screws i.e. patients who at first reported to be pain-free or at least considerably better in their low back pain, but then developed new low back pain often described as a “different pain” from the old one. When analysing this recurrence of pain, we did not report it as a complication. The reason for this was that in fusion surgery one expects implant removal in a few cases, though the frequency differs between clinics and points in time. Even if other surgeons would not have offered patients this procedure as often as was the case in the current study, this cause for reoperation is considered a common occurrence after instrumented posterior fusion. The question whether or not it is worth offering a patient this reoperation is debatable, but we intend to follow these patients separately in an attempt to find factors predicting a positive outcome. It has been reported<sup>130</sup> that in a material of patients fused for CLBP, only 25% of patients gained from implant removal. In six of the seventeen patients in the current study operated with instrumentation removal, a pseudarthrosis was later (after two-year follow-up) revealed and three of these patients were re-fused, one was decompressed at index-level and one had a TDR at an adjacent segment. We intend to follow separately the patients who had their instrumentation removed, to analyse whether it was worthwhile.

In patients treated with instrumented fusion, there is always a possibility to do something more if pain recurs,

namely to remove the implants. The corresponding option in patients treated with TDR with residual pain would be to offer the patient a fusion at the index segment, and that was also performed in this study. Whether or not re-fusion due to pseudarthrosis and implant removal in the fusion group balances reoperation in the TDR group will be reported in the future.

In the current study we found shorter operation times and shorter in-hospital stay in the TDR group compared to the fusion group, while there was no difference in blood loss.

Levin et al. also reported a shorter operating time in a TDR group compared to posterior fusion, but not a shorter hospital stay. On the other hand they had less blood loss in the TDR group<sup>92</sup>.

The length of hospital stay after the index episode was 1.8 days in the TDR group compared to 7.7 days in the fusion group. The text in the health economy study was unfortunately formulated so that it is easy to think that the only difference in length of hospital stay after the index episode is only due to implant removal, but the typical in-hospital stay for that procedure is two to three days.

The most frequent cause for reoperation in the TDR group was recurrent back pain. This pain was suspected to arise from the facet joints at the treated level when repeated facet blocks were positive. These patients were then fused at that level, though it is too early to analyse if this procedure altered their pain.

Apart from the positive effects on sex life and sexual function when back pain was reduced by the two different treatments, the current study also revealed a large impact of this type of back pain on patients' sex life prior to the treatment. The result gave no support for restrictions on using the anterior approach for spine surgery in men. The current study indicates that a modern careful and less traumatic technique (retroperitoneal approach) should be used instead of the transperitoneal approach.

Our results demonstrated a definite negative effect in males treated with posterior fusion on ability to have an orgasm. It was surprising, and must be confirmed. The only explanation for this result that we could think of was that the surgical trauma created some kind of weakness in the lumbar musculature resulting in severe fatigue.

Our measurements on pre- and two-year post-operative flexion-extension films demonstrated that the surgical goal was more often reached in the TDR group ( $p < 0.05$ ). This observation did not correlate with the clinical outcomes but this might differ with longer follow-up. We could not conclude from this investigation whether stiffness in fused segments was maintained due to the instrumentation or due to the desired bony fusion.

Preoperative mobility in the segments to be treated was less than in the normative database. Commonly "fear of pain on movement"<sup>99</sup> is attributed to this, but soft tissue changes surrounding the disc might also contribute<sup>89</sup>.

In our clinical study *in vivo*, the mobility in segments instrumented with a disc prosthesis increased compared to preoperative values, mainly in the extension domain. This is in contrast to a report from an *in vitro* study, where there was a small reduction in ROM but a significant reduction in extension after TDR<sup>33</sup>. Our findings of increased ROM contradict those of Siepe et al. who found that mobility decreased post-operatively<sup>125</sup>. Furthermore, they reported a significant correlation between preoperative disc height and postoperative ROM. Our study could not confirm their findings.

The degree of mobility in the artificial discs in our study was clearly larger than that measured preoperatively, but smaller than their design features and smaller when compared to healthy discs. This has been observed previously<sup>89</sup> and is explained as an adaptation/scarring of soft tissue that has taken place prior to treatment. There are no indications that a fully normal mobility of an artificial disc is required to give a potential reduction in ASD. Since ASD and also material component failure of disc prostheses or failure of its mobility, can take several years to develop, our study will continue until at least the ten-year follow-up.

Most of the TDRs that were judged to be non-mobile were found at L5–S1 level in the current study. Due to the high SD<sup>51</sup> at that level ( $2.3^\circ$ ) mobility had to exceed  $4.5^\circ$  to be rated as mobile. The anchorage of ligaments from L5 on S1 is much stronger than at other levels. Thus, some of these patients might have some mobility after all, but not exceeding  $4.5^\circ$ . Considering the results in the health economy study, if a TDR does not stay mobile, it might be argued that we have at minimum got a cheap fusion without having to worry about pseudarthrosis.

It is easy to over-compensate disc height with the TDR-method. However after fusion we observed in our study that the disc height was commonly lower than in the normative database.

In our health economy study, where the costs were related to the gain in life-quality and also the major change in sick-leave in the whole group, we could demonstrate, that the gain for the community from spine surgery with both these methods was large. The effects are also usually long lasting.

To the knowledge of the author, no health economy study has been performed to estimate the potential savings for society that could occur if patients with CLBP due to DDD were more frequently surgically treated. The results and conclusions of Ekman et al.<sup>38</sup> indicate that such a study could be beneficial. On the other hand, not everyone is willing to go through surgery, even if offered<sup>9</sup>.

Most health economy studies come to the conclusion that new treatments (in this study TDR) are better but more costly than the old treatment. Decision makers in the community have to evaluate whether the improved treatment effect is worth the extra cost.

In our study the new treatment, TDR, is less costly, or at least does not cost more than the old treatment, fusion, while having

a somewhat better effect in clinical outcome. This is a rare scenario. The positive difference in costs for the index treatment for TDR seen in our study was also noted by others<sup>92</sup>. The mean time on sick-leave after surgery was two months shorter in the TDR group than in the fusion group though, because of large variance this difference remained insignificant.

If TDR in the long run can reduce complications (ASD) associated with fusion surgery, its benefit will increase even more with time. On the other hand, if the materials in disc prostheses do not stand the test of time or facet-joints deteriorate so that fusion has to be undertaken, the increase in cost will be in the TDR group. If TDR-treated segments develop spontaneous fusion, no additional costs are expected.

From a community perspective, the two-year follow-up of this study is insufficient. The relatively short time between surgery and summary-of-costs follow-up implies that a high cost is spread out over just two years. However clinical experience indicates that the full economic gain from treating this patient group (CLBP) is to be expected first after many years, so a health economy study over a longer period is needed and is underway at our department.

We have to bear in mind that we were comparing a treatment method (fusion) that has been in use and developed over more than a century, to a method (TDR) that has been in limited use for a little more than twenty years. The new method will surely continue to develop over the years, as did the fusion technique. The theoretical advantage of surgical treatment of DDD with TDR as compared to fusion would be the maintenance of mobility in the treated segment. This would hypothetically reduce the frequency of ASD.

Already at two-year follow-up we found significant differences between the two treatment groups as concerns the clinical and radiological outcomes in favour of the TDR group. Some of the data did not show statistically significant differences between the two treatment groups; however there were tendencies in outcomes at two-year follow-up, all in favour of TDR. TDR treatment was not inferior to fusion treatment at any point investigated in this thesis.

### Acknowledgements

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## Conclusions

All differences observed in these current studies were in favour of TDR compared to fusion. TDR treatment was not inferior to fusion treatment at any point investigated.

- I.** More patients are totally pain-free after TDR compared to fusion.
- II.** There was no difference in complication rate or severity of complications between the two methods compared.
- III.** **A)** Sex life was to a large extent affected by CLBP prior to treatment. A negative effect of DDD on preoperative sexual function in men seems likely to have existed.  
**B)** Both treatments led to improvement in sex life. This showed a strong positive correlation to reduction in back pain.  
**C)** No men in any of the treatment groups reported persistent retrograde ejaculation postoperatively. Men in the fusion group more often had deterioration in their ability to have an orgasm.
- IV.** **A)** The surgical goals, mobility as opposed to fusion, were achieved in 89% in the TDR group and in 78% of the fusion group ( $p < 0.05$ ).  
**B)** Mobility in adjacent segments was within normative values in both groups after two years, but slightly more in the fusion group.  
**C)** Segments treated with TDR resulted in higher disc height, and fused segments in lower disc height postoperatively as compared to normative data.  
**D)** At two-year follow-up there was no significant correlation between the attainment of surgical goals and clinical outcome.
- V.** **A)** Health-care costs were lower for TDR.  
**B)** Preoperatively 30% of the patients in this study were working. At two-year follow-up 74% were working.  
**C)** TDR was at least as cost-effective as fusion.

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