

The following list recommends future directions for spine research. It is derived from gaps identified in the spine literature during clinical guideline development.

Special Note to Researchers: Studies incorporating the concept and evaluation of value are encouraged to help further develop evidence in the spine field related to the relationship between cost and quality. Studies evaluating treatment outcomes should utilize validated outcome measures and include results specific to each of the treatment methods implemented in the study for all subgroups studied.

Antibiotic Prophylaxis in Spine Surgery

Efficacy

Use of Antibiotic Prophylaxis vs. Patients Who Do Not Receive Prophylaxis

- Further study is needed on the use of collagen or other carriers for local antibiotic treatments.
- A case controlled study utilizing available national databases to determine the relative efficacy of antibiotic prophylaxis in single-level, instrumented cases.
- A series of randomized, controlled studies each dealing with a specific subpopulation defined by diagnosis and procedure.

Protocol

- Prospective, randomized, clinical trials to compare the efficacy of cephalosporins to aminoglycosides and other antibiotics.
- Prospective, randomized, clinical trials to compare different timing and dosage protocols, for example, single perioperative dose versus multiple dose protocols.
- Prospective, comparative drug studies to determine optimal antibiotic prophylaxis regimen.
- Prospective, comparative studies to determine optimal dosing regimens for antibiotic prophylaxis.
- A case controlled study utilizing available national databases to determine the relative efficacy of different antibiotic prophylactic protocols in single-level, uninstrumented cases.
- A case controlled study utilizing available national databases to determine the relative efficacy of different antibiotic prophylactic protocols in single-level, instrumented cases.
- Case controlled studies to evaluate rates of polymicrobial infection stratified by comorbidities to identify other high risk populations.
- Prospective, randomized studies to evaluate the effect of broad spectrum antibiotic coverage in reducing infection rates in various high risk populations treated with instrumented fusion.

Redosing

- A case controlled study utilizing available national databases to determine the relative efficacy of redosing antibiotic prophylaxis in specific patient populations undergoing spine surgery.
- A series of randomized controlled studies evaluating dosing regimens. Each study could address a specific subpopulation defined by diagnosis, procedure and comorbidity.

Discontinuation

- Controlled studies comparing infection rates in spinal surgical patients who received antibiotics which were discontinued at 24 hours as compared with groups who received antibiotics for a longer period of time.

Wound Drains

- Controlled studies comparing infection rates in nonfusion and nonimplanted spinal surgical patients with drains and discontinuation at 24 hours as compared with longer duration prophylaxis.
- Controlled studies comparing infection rates in spinal surgical patients receiving spinal implants with drains and discontinuation at 24 hours as compared with longer duration prophylaxis.

Body Habitus

- Prospective, randomized clinical trials to evaluate the effect of antibiotic choice and altered dosing on infection rates in obese patients.

Comorbidities

- Prospective, randomized clinical trials to evaluate the effect of antibiotic choice and altered dosing on infection rates in potentially high risk patients.
- A case controlled study to help identify other potential comorbidities leading to higher infection rates in patients undergoing spine surgery.

Antithrombotic Therapies in Spine Surgery

Efficacy

- A randomized, controlled trial comparing mechanical prophylaxis alone (ie, pneumatic compression boots or compression stockings) with combined LMWH and mechanical prophylaxis in high-risk patients to assess the respective incidence of DVT, PE, neurological deterioration secondary to epidural hematoma, postoperative bleeding and wound complications.
- A randomized, controlled trial comparing mechanical prophylaxis alone (ie, pneumatic compression boots or compression stockings) with combined low-dose warfarin and mechanical prophylaxis in high-risk patients to assess the respective incidence of DVT, PE, neurological deterioration secondary to epidural hematoma, postoperative bleeding and wound complications.
- A prospective, uncontrolled, prognostic, multicenter study of a high number of patients undergoing a wide variety of spine surgeries to quantify the relative risk of a number of suspected predisposing factors for VTE that include, but not be limited to, length of surgery, number of levels fused, underlying diagnosis, traumatic injury, paralysis and SCI. In addition, the relative risks of postoperative neurological deterioration from epidural hematoma, bleeding, wound complications, and transfusion requirements should be scrupulously defined for each subgroup.

Chemoprophylaxis

- A randomized, controlled trial of LMWH vs. heparin as a bridge therapy for patients on long term warfarin prophylaxis for cardiac or other vascular conditions.
- A comparative study identifying the risks of perioperative bleeding complications in spinal surgery patients with clopidogrel-coated stents compared with those taking ASA and controls.
- A comparative study investigating the rate of bleeding complications in patients discontinuing clopidogrel ten days, seven days and one day prior to elective spinal surgery.
- A prospective study investigating optimum duration of postoperative prophylaxis comparing three groups of spine surgery patients treated with LMWH, ASA or clopidogrel for one week and another three groups of patients treated with LMWH, ASA or clopidogrel for four weeks.
- A comparative study investigating the incidence of bleeding complications in spinal patients receiving LMWH immediately postoperatively with another group of patients receiving LMWH three days postoperatively.

Wound Complications

- Controlled studies documenting rates of wound complications in spinal surgical patients who received specific chemoprophylaxis protocols. Data recorded for each patient should include type of procedure as well as specific chemoprophylaxis protocol (chemoprophylaxis agent, dosage, timing and duration).

Degenerative Lumbar Spondylolisthesis

Natural History

- Prospective study of untreated patients, all with degenerative lumbar spondylolisthesis without neurologic compromise to provide Level I evidence regarding the natural history of the disease. This study could include stratification as to the type of spondylolisthesis and evaluate progression of radiographic severity and clinical severity over time.
- Any systematic study of patients with untreated spondylolisthesis who presented with varying degrees of neurologic deficit to provide evidence regarding the natural history of the disease in this patient population. For example, defining and following a group of patients with lumbar spondylolisthesis and sensory deficits as compared with those who present with motor deficits that have not been treated would yield Level I evidence.

History and Physical Exam

- A high quality, prospective study identifying specific aspects of the history and physical examination and characterizing the subgroups of patients with degenerative spondylolisthesis. Ideally the study would enroll a large number of patients, screen for symptomatic and asymptomatic degenerative lumbar spondylolisthesis, and have greater than 80% follow-up. Subgroups for evaluation could include patients with or without instability, radiculopathy, neurogenic intermittent claudication and back pain.

Diagnostic Tests

- A prospective, appropriately powered study assessing the utility of supine (gold standard), standing and dynamic flexion-extension lateral radiographs in the evaluation of patients with degenerative spondylolisthesis. NOTE: These studies should assess a set of diagnostic criteria established a priori.
- A prospective, appropriately powered study assessing the utility of supine recumbent (gold standard), axial loaded and positional MRI in the detection and evaluation of stenosis via analysis of the dural sac area in patients with degenerative spondylolisthesis. NOTE: These studies should assess a set of diagnostic criteria established a priori.

Outcome Measures

- Further studies are needed to validate additional outcome measures (Stenosis Bothersome Index, LBP Bothersome Index, Oxford Claudication Score, Shuttle Walking Test, JOA and calculated Recovery Rate) for the treatment of degenerative lumbar spondylolisthesis. Currently, the best outcome measure for degenerative spondylolisthesis with symptoms of spinal stenosis is the ZCQ/SSS as a disease-specific outcome tool. General health outcome tools that are appropriate for degenerative lumbar spondylolisthesis are the SF-36 and ODI.
- Degenerative lumbar spondylolisthesis with back pain alone needs to be defined as a stand-alone clinical entity by outcomes research. The use of these outcome measures in this subgroup of patients needs to be studied.

Medical/Interventional Treatment

- The SPORT study demonstrated the intrinsic difficulties in conducting RCTs comparing surgical to medical/interventional treatment in the North American patient population. It is unlikely that higher quality data are achievable for the comparison of surgical and medical/interventional treatment. Future studies are needed to assess the effects of medical, noninvasive interventions for degenerative lumbar spondylolisthesis. These studies should include an untreated control group when ethically possible and should include results specific to each of the medical/interventional treatment methods implemented, presenting results stratified by patient symptomatology (e.g., axial back pain only, combination of axial back pain and radiculopathy).
- A randomized controlled study comparing the benefits of physical therapy with directional preference versus nonpreferential therapy for the treatment of degenerative lumbar spondylolisthesis.

Surgical Treatment

- Independent randomized controlled trials to validate what appears to be an effective and minimally invasive means (interspinous spacers) of decompressing the spinal canal in patients with symptomatic spinal stenosis and degenerative lumbar spondylolisthesis.
- A high quality randomized controlled trial to provide meaningful information about the clinical benefits of achieving a solid fusion in patients treated with instrumented and noninstrumented fusion for symptomatic spinal stenosis and degenerative lumbar spondylolisthesis. This study should utilize validated, functional, disease-specific outcome measures with long-term follow-up of four years or more.
- A high quality RCT comparing decompression with instrumented posterolateral fusion to decompression with 360° (circumferential) instrumented fusion.
- Future long-term studies of the effects of surgical interventions for patients with symptomatic spinal stenosis and degenerative lumbar spondylolisthesis are needed and should include an untreated control group, when ethically feasible. Continued follow-up of patients already enrolled in ongoing randomized controlled trials or prospective comparative studies will yield higher quality data regarding the relative efficacy of surgery compared to medical/interventional treatments.
- Future long-term outcome studies are necessary to compare different surgical techniques for the treatment of patients with symptomatic spinal stenosis and degenerative lumbar spondylolisthesis.

Degenerative Lumbar Spinal Stenosis

Natural History

- A prospective study of patients with symptomatic degenerative lumbar spinal stenosis without treatment, notwithstanding nonprescription analgesics, would provide Level I evidence regarding the natural history of this disorder. Unfortunately, at this time, following symptomatic patients long-term with no intervention is unlikely to occur.
- A systematic study reviewing patients with untreated symptomatic degenerative lumbar spinal stenosis would provide evidence regarding the natural history of the disease in this patient population.

History and Physical Findings

- A sufficiently powered observational study of the predictive value of historical and physical findings in patients with the lumbar spinal stenosis, as defined by this guideline, is proposed. The study should allow for a subgroup analysis of the subsets of patients with neurogenic claudication and radiculopathy.
- A prognostic study with long-term follow-up of up to 10 years could be performed on the cohort of spinal stenosis patients defined in Study #1.
- A prognostic study to clarify the association of gait abnormalities, posture, balance and fall risk in patients with lumbar spinal stenosis.
- A prognostic study on the reliability of patient-reported dominance of lower extremity pain and low back pain.

Diagnostic Tests

- Develop reliable and reproducible criteria for the diagnosis by cross-sectional imaging of central, subarticular recess and foraminal stenosis.
- Perform additional interobserver and intraobserver variability studies with MRI and CT myelography using dural sac area as a measure of central canal stenosis, and utilizing measures incorporating neural impingement as measures of lateral and foraminal stenosis.
- Future studies assessing the effectiveness of therapeutic interventions should utilize previously defined clinical measures of Lumbar Spinal Stenosis, and state of the art measures of central, lateral recess and neural foraminal stenosis on MRI, CT and CTM, and should report subgroup analyses for central/neurogenic claudication versus lateral stenosis/radiculopathy.
- Perform additional prospective studies evaluating the significance of additional findings on axial loaded cross-sectional imaging on patient prognosis and surgical decompression in patients with neurogenic intermittent claudication and radiculopathy.
- Perform additional prospective studies addressing the utility of paraspinous mapping and electrodiagnostic testing in the evaluation of patients with clinical and radiologic degenerative lumbar spinal stenosis. Future studies should also address the value of these tests in the evaluation of patients with equivocal clinical signs and symptoms, and patients with confounding diagnoses such as diabetes. Future studies should focus on the ability of paraspinous mapping and electrodiagnostic testing to improve outcomes with surgical decompression.

Medical/Interventional Treatment

- Future studies of the effects of medical, noninvasive interventions for lumbar spinal stenosis should include an untreated control group when ethically possible.
- Future outcome studies of lumbar spinal stenosis should include results specific to each of the medical/interventional treatment methods.
- A large, double-masked, randomized controlled trial with a long-term observation period to examine the potential benefits of intramuscular calcitonin for the treatment of lumbar stenosis.
- An RCT with long-term follow-up and validated outcome measures would assist in providing evidence to assess the efficacy of physical therapy in the treatment of lumbar spinal stenosis. Ideally, this would be compared to an untreated control group. We recognize this may be a difficult or unethical study to propose over the long term. Other active treatment groups could be substituted as a comparative group. The physical therapy program should be standardized and should include exercise and education at a minimum, and could include separate cohorts of manual therapy and other modalities as well.

- If ethically possible, future studies should include a controlled trial comparing manipulation to natural history of lumbar spinal stenosis using standardized techniques and validated outcome measures.
- Future studies should utilize validated outcome measures to compare manipulation to other medical/interventional treatments for spinal stenosis, and should assess long-term effectiveness and cost effectiveness.
- A large double-masked, randomized controlled clinical trial with at least one-year follow-up in patients with unilateral leg pain from lumbar spinal stenosis treated by fluoroscopically-guided contrast-enhanced transforaminal epidural steroid injections in which the control group receives saline placebo injections.
- A large double-masked, randomized controlled clinical trial with at least two-year follow-up in patients with neurogenic claudication from lumbar spinal stenosis treated by fluoroscopically-guided interlaminar or caudal epidural steroid injections in which the control group receives saline placebo injections.
- An appropriately powered study is proposed containing three groups with symptomatic lumbar spinal stenosis comparing soft bracing, rigid bracing and untreated controls (no bracing). Outcome measures could include the ZCQ, VAS, walking distance and a validated, health-related quality of life measure such as the SF-36 or ODI.
- Prospective, RCTs with validated outcome measures are needed to evaluate efficacy of ancillary treatments such as acupuncture, TENS, traction and electrical stimulation in a comparative manner. When ethical, evaluating the efficacy of these treatments compared to untreated controls would be ideal. Alternatively, this can be used as a comparative group in an RCT with PT, injections and/or medications.
- Future long-term studies of the effects of medical, noninvasive interventions for lumbar spinal stenosis should include an untreated control group.
- Future long-term outcome studies of lumbar spinal stenosis should include results specific to each of the medical/interventional treatment methods.

Surgical Treatment

- A large, multicenter, three-arm, randomized, controlled trial using a well-defined group of patients with moderate clinically symptomatic stenosis, comparing lumbar decompression to a well-defined medical/interventional treatment program and / or a natural history group of untreated patients is needed. A large, multicenter, three-arm, randomized, controlled trial using a well-defined group of patients with mild to moderate clinically symptomatic stenosis, comparing the use of interspinous spacers to a microlaminotomy decompression and / or a well-defined medical/interventional treatment program is needed.
- Future long-term studies of the effects of surgical interventions for lumbar spinal stenosis should include an untreated control group, when ethically feasible.
- Future long-term outcome studies of lumbar spinal stenosis should include results specific to each of the surgical treatment methods.
- Large cohort studies utilizing transparently unbiased databases, such as exist in Scandinavia and large medical systems (eg HMOs), could serve to validate these long-term results.

Cervical Radiculopathy from Degenerative Disorders

Natural History

- A prospective study of patients with cervical radiculopathy from degenerative disorders without treatment, notwithstanding non-prescription analgesics, would provide Level I evidence regarding the natural history of this disorder.
- A systematic study of patients with untreated cervical radiculopathy from degenerative disorders would provide evidence regarding the natural history of the disease in this patient population.

History and Physical Findings

- Further studies are needed to demonstrate the positive predictive value of specific symptoms and physical exam findings in patients with confirmed cervical radiculopathy to demonstrate their usefulness in predicting a good outcome with conservative or surgical treatment.

Diagnostic Tests

- Studies evaluating the accuracy of MRI, CT and CT myelography in detecting and characterizing compressive le-

sions in the cervical spine in patients with cervical radiculopathy should be repeated using state of the art equipment and imaging techniques and should implement surgical findings and outcomes as gold standards.

- Further studies should be done to evaluate the contribution of EMG to the evaluation of cervical radiculopathy patients with discordant MRI findings and clinical findings using surgical findings and outcomes as gold standards.
- Further studies should be done evaluating the contribution of SNRB to the evaluation of cervical radiculopathy patients with discordant MRI findings and clinical findings, and to the evaluation of cervical radiculopathy patients with findings on MRI at multiple levels ipsilateral to the patient's symptoms using surgical findings and outcomes as gold standards.
- Studies should be done evaluating the contribution of dynamic upright cervical spine MRI to the evaluation of and long term outcome of patients undergoing surgical decompression for cervical radiculopathy with attention to the following question: Does the presence of dynamic central canal stenosis at an adjacent level affect the long term outcome of patients undergoing surgical decompression using an anterior approach with fusion versus a motion preserving posterior approach?

Outcome Measures

- Disease-specific outcome measures like the PSFS and the HSQ have been developed and seem to be useful in assessing outcome for the treatment of cervical radiculopathy from degenerative disorders. These measures are limited in that they have not been widely used or accepted. Outcome measures such as these need to be incorporated into Level I studies to confirm their validity and to establish themselves as acceptable research tools to quantitate outcome after cervical radiculopathy from degenerative disorders.

Medical/Interventional Treatment

- Future studies of the effects of pharmacological treatment in the management of cervical radiculopathy from degenerative disorders should include an untreated control group when ethically possible.
- Future outcome studies including patients with cervical radiculopathy from degenerative disorders treated only with pharmacological treatment should include subgroup analysis for this patient population.
- Future studies of the effects of physical therapy/exercise in the management of cervical radiculopathy from degenerative disorders should include an untreated control group when ethically possible.
- Future outcome studies including patients with cervical radiculopathy from degenerative disorders treated only with physical therapy/exercise should include subgroup analysis for this patient population.
- Future studies evaluating the effects of emotional, cognitive and work-related issues would add to our understanding of how these factors affect outcomes in patients with cervical radiculopathy from degenerative disorders.
- Future studies of the effects of manipulation/chiropractics in the management of cervical radiculopathy from degenerative disorders should include an untreated control group when ethically possible.
- Future outcome studies including patients with cervical radiculopathy from degenerative disorders treated only with manipulation/chiropractics should include subgroup analysis for this patient population.
- Future studies of the effects of manipulation/chiropractics in the management of cervical radiculopathy from degenerative disorders should include data and discussion about any complications associated with treatment.
- Future studies of the effects of epidural steroid injections in the management of cervical radiculopathy from degenerative disorders should include an untreated control group when ethically possible.
- Future outcome studies including patients with cervical radiculopathy from degenerative disorders treated only with epidural steroid injections should include subgroup analysis for this patient population.
- Future studies of the effects of epidural steroid injections in the management of cervical radiculopathy from degenerative disorders should include data and discussion about any complications associated with treatment.
- Future studies of the effects of ancillary treatments in the management of cervical radiculopathy from degenerative disorders should include an untreated control group when ethically possible.
- Future outcome studies including patients with cervical radiculopathy from degenerative disorders treated only with ancillary treatments should include subgroup analysis for this patient population.
- Future studies evaluating the effects of emotional, cognitive and work-related issues would add to our understanding of how these factors affect outcomes in patients with cervical radiculopathy from degenerative disorders.

Surgical Treatment

- A prospective, multicenter randomized controlled trial (RCT) with minimum two year follow-up comparing surgical to medical/interventional treatment for the treatment of cervical radiculopathy from degenerative disorders would yield invaluable information regarding the relative outcomes of these two treatment options.
- Future studies evaluating the effects of emotional, cognitive and work-related issues would add to our understanding of how these factors affect outcomes in patients with cervical radiculopathy from degenerative disorders.
- Prospective, blinded, RCT comparing clinical outcomes and radiographic alignment of patients treated for cervical radiculopathy due to single level degenerative disease with ACD compared with ACDF with a uniform surgical technique would generate important information about the relative value of preserving normal alignment.
- A well designed, prospective RCT to compare radiographic and clinical outcomes following ACDF with or without a plate for degenerative cervical radiculopathy would generate meaningful data regarding the potential long term benefits of preserving or restoring sagittal alignment. There should be two cohorts, one with single level disease, and one with multilevel disease.
- Prospective, RCT with long term follow up to evaluate clinical outcomes, perioperative complications, and long term success including need for revision surgery following treatment of degenerative cervical radiculopathy with posterior foraminotomy versus ACDF. The study group would consist of foraminal stenosis only and should include two separate cohorts, including “soft disc” herniation and hard disc or spondylotic disease.
- Continued long term follow-up of patients currently enrolled in previously reported RCTs is necessary to determine if purported advantages of TDA compared with ACDF can be validated, with particular focus on validated clinical outcomes, revision surgery and adjacent segment disease. Subgroup analysis should include soft disc compared with hard disc and foraminal compared with paracentral pathology for cervical radiculopathy patients.
- Additional independent, masked, prospective RCTs comparing ACDF to TDA for the treatment of cervical radiculopathy from degenerative disorders would add substantial unbiased validation to the results of the investigational device exemption (IDE) studies.
- An adequately powered, prospective, comparative study of patients treated with ACDF, ACD, TDA and PLF followed for greater than four years and assessed with validated outcome measures would yield useful information about the long term outcomes of surgery for cervical radiculopathy from degenerative disorders.