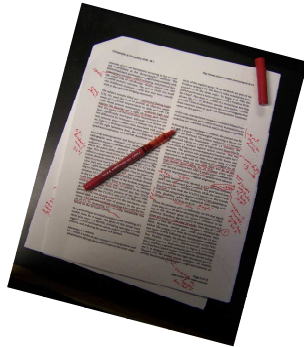


The Critical Appraisal



- **What is a “Journal Club?”**
- **Overview of the critical appraisal**
- **Critically appraising a clinical trial in a journal club**



What is a Journal Club?

- An educational meeting in which a group of individuals read, evaluate and discuss current articles from the biomedical literature
- A collective forum to provide a venue to keep up with the literature
- One of the most effective means by which students and professionals keep up with current biomedical literature
- Evidence based practice in action



What is a Journal Club?

- Classic learning and information sharing format
- Focused on current, (biomedical) research literature
- “Just-in-time” delivery
- **Critically appraised** information with **commentary** and **discussion** for applicability and relevance
- Can be used as a professionally reviewed **secondary evidence source**



What is a Journal Club?

- Earliest mention: mid 1800s
 - British surgeon (the late Sir James Paget), described sitting over the baker's shop near London's St. Bart's Hospital gate
- First formal established journal club: 1875
 - Sir William Osler at McGill University, Montreal
 - original purpose: share and distribute professional periodicals “to which he could ill afford to subscribe.”
- First formal journal club at a professional complementary and alternative medical school: Sept. 2006
 - National University of Health Sciences



Successful Journal Clubs in Professional and Continued Education include:

- The well-built, clinical question
- “Medical informatics:” search & access logic and strategy
- A critical appraisal
- Commentary and discussion practiced critical analysis



- Slawson DC. Acad Med. 2005 Jul;80(7):685-9.
- Atzema C. Ann Emer Med 2004;44(2):174.
- Shilling K. Fam Med 2006;38(2):126-32.

Benefits of a Critical Appraisal

- An analytical summary and evaluation of a research study
- Standard approach: recognize important information
- Standard format: easily digested, a quick read
- Usable by professionals in busy practices
as summarized, synthesized evidence
- Publishable quality
- Rapidly accessible, archived for your use



Critical Appraisals: EBP in Action

- *Several* critically appraised *primary research papers* focused on the same patient oriented clinical question = **CAT**
- *Several* summarized Critical Appraisals focused on the same topic = **Best Evidence for a Topic (BET)**



Really useful places to find accessible, patient focused CATs and BETs

- **Critically Appraised Topics**
 - University of North Carolina – Chapel Hill Dept. of Internal Medicine <http://www.med.unc.edu/medicine/edursrc/catlist.htm>
 - Center for Evidence Based Medicine Oxford University <http://www.minervation.com/cebm2/cats/allcats.html>
- **Best Evidence Topics (and linked Critical Appraisals)**
 - Emergency Department of Manchester Royal Infirmary, UK <http://www.bestbets.org/>
- **Journal Clubs**
 - American College of Physicians (ACP) Journal Club <http://www.acpjic.org/> available through NUHS EBSCOhost (search & browse)
 - Journal Review <http://www.journalreview.org/>

The Critical Appraisal

Let's look at a Critical Appraisal...



Back Pain Therapies: Patient Scenario

- Evidence based practice begins and ends with a patient
- Describe the case or problem that focused your clinical question and structured search
- Present a patient focused clinical question (PICO)



Back Pain Therapies: Patient Scenario

James, 32 year old male, technical sales manager who drives long distances (or at least for long periods of time) and is a frequent flier for his job, has been Seeing you for neck and back issues for over two years on a fairly regular basis.



In addition to working from the car and plane, he has a home office and uses a laptop. You and he have discussed work place ergonomics as well as exercise and stretching to alleviate chronic neck and back pain.

On a recent visit, he tells you he heard on the TV news that chronic back and neck pain causes depression -- or was it vice versa? -- and that chiropractic and alternative care that relieves the pain can relieve depression. He asks, "Do you think that this back and neck thing could be causing me to feel blue lately? Or do you think mid-winter blues are causing this pain in my lower back and neck? My colleague just had lumbar disk surgery and feels great. I'm not so excited about surgery. Should we be doing something different?"

He says after hearing that news report, he's been looking on the internet to see what might help with the chronic pain and lift his mood.



Critical Appraisal: Back Pain Therapies

PICO Question

| | Patient, population, problem | Intervention | Comparison | Outcome |
|-----------------|---|---|--|--|
| Consider | 32 yo WM chronic neck / back pain spine, lumbar disk, Stenosis, sciatica, etc. | CAM therapy chiropractic acupuncture "physical therapy" nonsurgical nonoperative botanical herbal massage | Prescription drugs Opioid compounds surgery massage... alternative therapy treatment | to treat / relieve chronic (neck / back) pain (mild) depression spine conditions |
| PICO | For [P= adult patients with chronic (neck / back / spine / lumbar) pain / specific diagnosis], is [I= conservative / nonoperative treatment / botanical therapy / acupuncture] as effective as [C= surgery] to [O= alleviate pain / treat symptoms of mild depression]? | | | |



Search strategy and results:

- List separate searches, queries
- Summarize
- Explain what you did
- Searching, finding, accessing is essential to the evidence-based practitioner.
- Bullet point how full text was located
- Communication skills are essential to applying and assessing evidence

Starting an effective search

Go to the source your patient recalls ...

- www.google.com
 - NBC 5 health
 - Chiropractic low back pain
 - <http://www.nbc5.com/health/10536565/detail.html>



The screenshot shows a Windows Internet Explorer browser window displaying a news article on the NBC5 website. The article title is "Back Pain Caused, Treated Many Ways" and the author is Edward Dykhuizen. The article text describes a 28-year-old graduate student named Erin who has chronic upper back problems and found relief through chiropractic care and acupuncture. The browser's address bar shows the URL: http://www.nbc5.com/health/10536565/detail.html. The page layout includes a search bar, navigation links, and an advertisement for Allstate on the right side.

Read, follow ...

Village Live

About NBC 5

About Us

NBC5 News Today

Marketplace

Classified Ads

Marketplace

2006 Healthy Lifestyle Expo

Junior Year Abroad

Education

Family

Food

Automotive

Employment

House And Home

Financial

Real Estate

Travel

Lottery Results

According to [an overview of back pain from the National Institute of Health](#), the back is uniquely complicated. It is made up of dozens of bones, muscles and nerves, all of which must be in harmony. A slight strain in one muscle or a slight misalignment between two bones can constrict a nerve, causing back pain.

Chiropractors such as Lederer take X-rays to ensure that patients' spines are in need of realignment.

"What I see most often in the X-rays I take are spinal degeneration, osteoarthritis, degenerative disc disease or other conditions," he said.

Treating The Pain

Surgery may be necessary for more serious cases of back pain, but Lederer emphasized that it is only an option after more conservative options have been exhausted. He cited a [recent article in the Journal of the American Medical Association](#) that showed back surgery and certain exercise programs yield about the same results.

Manipulation from a chiropractor is a much less drastic method for helping resolve the imbalance that causes the pain. Chiropractors go through years of training to learn how to adjust joints enough to restore a normal range of motion.

Spinal manipulation -- often accompanied by the "pop" of air being moved from a joint -- is not a full solution by itself. According to Lederer, "chiropractic care now and exercise later" is the best approach. He gives patients exercises to perform that will strengthen back muscles, and he also emphasizes the need for periodic adjustments.

Long-Term Solutions

Of course, if your job is contributing to your back problems, it may be necessary to change the conditions in which






Follow a link to Website #3:

http://www.ninds.nih.gov/disorders/backpain/detail_backpain.htm

Low Back Pain Fact Sheet: National Institute of Neurological Disorders and Stroke (NINDS) - Wi...

http://www.ninds.nih.gov/disorders/backpain/detail_backpain.htm

File Edit View Favorites Tools Help

Low Back Pain Fact Sheet: National ...

Home Feeds (0) Print Page Tools Help

Accessible Version | Skip Menu

Enter Words Here Search

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

Home About NINDS Disorders Funding & Research News & Events Find People Training

You are here: Home > Disorders > Back Pain

Low Back Pain Fact Sheet

More about Back Pain

- Studies with patients
- Research literature
- Press releases
- Disclaimer
- Contact Us
- My Privacy

NINDS is part of the National Institutes of Health

Get Web page suited for printing

Email this to a friend or colleague

Request free mailed brochure







Print-friendly version

Email this page

Table of Contents (click to jump to sections)

- What structures make up the back?
- What causes lower back pain?
- Who is most likely to develop low back pain?
- What conditions are associated with low back pain?
- How is low back pain diagnosed?
- How is back pain treated?
- Can back pain be prevented?
- Quick tips to a healthier back
- What research is being done?

Affiliation? Research? Current information?



Follow a link to a research article:

<http://jama.ama-assn.org/cgi/content/abstract/296/20/2451>

The screenshot shows a web browser window with the URL <http://jama.ama-assn.org/cgi/content/abstract/296/20/2451>. The page is the abstract for a research article in JAMA. The article title is "Surgical vs Nonoperative Treatment for Lumbar Disk Herniation: The Spine Patient Outcomes Research Trial (SPORT) Observational Cohort". The authors listed are James N. Weinstein, DO, MS; Jon D. Lurie, MD, MS; Tor D. Tosteson, ScD; Jonathan S. Skinner, PhD; Brett Hanscom, MS; Anna N. A. Tosteson, ScD; Harry Herkowitz, MD; Jeffrey Fischgrund, MD; Frank P. Cammisa, MD; Todd Albert, MD; Richard A. Deyo, MD, MPH. The abstract text includes a context paragraph, an objective, design, setting, and patients section, and an interventions section. The main outcome measures are changes from baseline in the Medical Outcomes Study Short-Form Health Survey (SF-36) bodily pain and physical function scales. The browser's taskbar at the bottom shows various applications like Microsoft Word, iTunes, and Internet Explorer.

Search strategy and results:

Search Engines / Program(s) & Databases searched

- 1) Natural Standards (www.naturalstandards.com)
- 2) Entrez PubMed
- 3) EBSCOhost: CINAHL, AMED

Query used (Key Search Terms, Operators used and limits)

- 1) Conditions: lumbar, low back, cervical and neck key word search
- 2 & 3) (back OR lumbar OR neck) pain surgical > (Limits: human, date: 2005-2007, peer reviewed)
- 2) PubMed Clinical Query: therapy, narrow, specific

Limits and Special Techniques:

- Patient info; local TV channel website Google search back pain
- MeSH for "surgery" led to nonoperative; Boolean operators: included OR for multiple conditions
- Limits used to revise search: published in the last 2 years, Humans, English, core clinical journals, complementary medicine, adult:19-44 yrs

Search strategy and results:

Search results:

- Google search TV website: links to 1 website, 1 article
- PubMed with limits: 69 articles, 6 reviews
- EBSCOhost 149 articles, 14 reviews

Selection rationale:

- JTASS JAMA peer reviewed, publishing history, professional association; authors have a publishing track record in spine research, surgery; Title key words focus on surgery versus non-operative for lumbar disc herniation; outcomes measured: pain (patient), physical disability; secondary sciatica, return to work, quality of life; large subject population; strong study design (randomized clinical trial)

How full text was accessed:

- Website link to JAMA related article, available as free full text; PubMed related articles in NEJM, JAMA available through NUHS EBSCOhost and LRC password list



Surgical vs nonoperative treatment for lumbar disk herniation: the Spine Patient Outcomes Research Trial (SPORT): a randomized trial.

Weinstein JN, Tosteson TD, Lurie JD, Tosteson AN, Hanscom B, Skinner JS, Abdu WA, Hilibrand AS, Boden SD, Deyo RA.



JAMA 2006 Nov 22;296(20):2441-50.

http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=ShowDetailView&TermToSearch=17119140&ordinalpos=7&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum



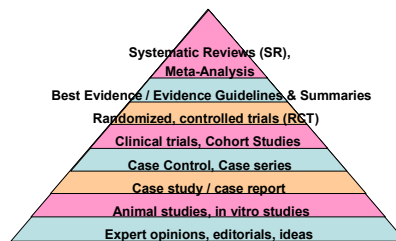
Study objectives and hypothesis

- State the purpose, objectives and hypothesis
- Using your words, what was the research question and objective(s) of the study?
- Was the purpose of the study conveyed plainly and rationally?
- Were the objectives of the study clearly stated?
- Was the hypothesis / null hypothesis explained



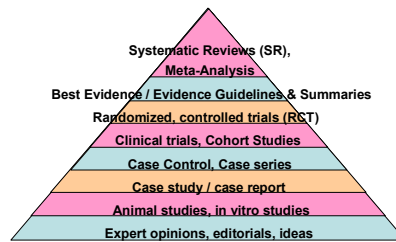
Study objectives and hypothesis

- SPORT: Spine Patient Outcomes Research Trial
- Initiated March 2000
- Purpose: to compare the outcomes of surgical and nonoperative therapies for lumbar disk herniation (LDH), spinal stenosis, or degenerative spondylolisthesis
- Multiple sub-studies to evaluate specific conditions, specific surgical interventions



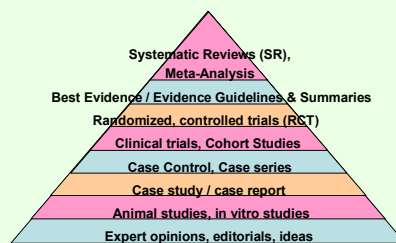
Study objectives and hypothesis

- For LDH and discectomy: Weinstein JN, et al. Surgical vs nonoperative treatment for lumbar disk herniation: the Spine Patient Outcomes Research Trial (SPORT): a randomized trial. JAMA 2006 Nov 22;296(20):2441-50.
- Objective: To assess the efficacy of standard open discectomy with involved nerve root examination
- Stated in abstract
- Hypothesis not clear 🚫
- Null hypothesis:
 - Surgery is not as effective as nonoperative treatments 🚫
- Initial "intention to treat" analysis



Type of study, study design, strength

- Was the study design stated and adequately described? What is the stated study design?
- Considering the strengths and limitations of the study design, is it suitable for the objectives?



Study Design & “Level of Evidence”

“Level” of evidence



Type of study, study design, strength

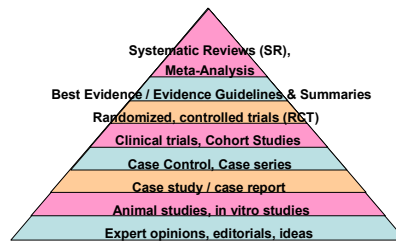
“Best” study design

- Therapy: randomized controlled trial (RCT), randomized clinical trial (comparison, no zero control, placebo), strong cohort with defined control
 - Other study designs are valid, not as “strong”
- Prognosis: cohort studies with untreated / exposed control, case control design, strong, well-defined case series
- Diagnosis: cohort study with strong reference standard, strong all-or-none case series
- Etiology / Harm: RCT, prospective cohort, case control with well defined control / comparison



Type of study, study design, strength

- Therapy study
- Randomized clinical trial design
- Two “cohorts” or groups: surgery and nonoperative (heterogeneous therapies) 🇸🇬
- Strong study design for therapy study
- Caution that therapy for comparison group (cohort) is not well defined 🇸🇬



| | Randomized Controlled Trial (RCT) | Cohort Design |
|----------------------------|--|---|
| Populations studied | Highly selected populations recruited on the basis of detailed criteria Treated at selected sites | Diverse populations observed in a range of settings |
| Allocation to intervention | Based on chance Controlled by investigators | Not randomized Based on decisions made by providers or patients |
| Outcomes | Primary outcomes determined before patients enrolled in study; focused on predicted benefits and risks | Can be defined after the intervention (exposure) Can include rare or unexpected events |
| Follow-up | Prospective studies; often short follow-up due to costs and pressure to produce timely evidence | May rely on existing experience (retrospective studies) Can provide opportunity for long follow-up |
| Analysis | Analysis is straightforward | Sophisticated multivariate techniques may be required to deal with confounding |
| Validity | Internal validity enhanced by minimizing selection bias and confounding | Vulnerable to selection bias - groups may differ in factor related to outcome |

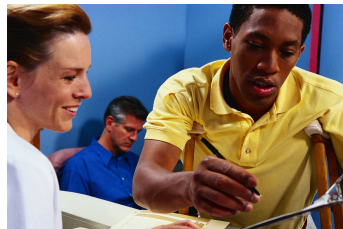
Methods: Subjects / Participants / Patient / Population

- Focus on PICO components, but don't leave out info that might affect validity
- Method of selection
- Selection population. Bias?
- How were patients recruited? Bias?
- Inclusion criteria / exclusion criteria
 - Generalizable? Too broad, too narrow?
- "Real life" circumstances of study? (relevance)
- Baseline differences?
 - Experimental and control groups start with similar prognosis
 - More homogeneity is stronger
- Sample size adequate to support measurement of outcomes?
- Rationale for choosing sample size?



Methods: Subjects / Participants / Patient / Population

- Recruited from population presenting at 13 multidisciplinary spine clinics 🇺🇸
- 11 states (US)
- 501 enrolled of 1991 eligible
- Corresponding to similar, earlier study (Maine Lumbar Spine Study; refs provided)
- Sample size calculations allowed up to 20% missing data
- No allowance for non-adherence 🇺🇸



Weinstein JAMA, Nov 22/29, 2006 Vol 296:20

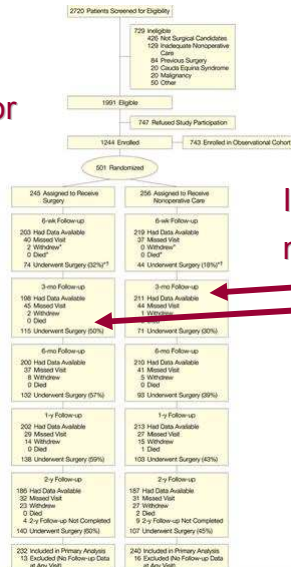
Figure 1. Flow Diagram of the SPORT Randomized Controlled Trial of Disk Herniation: Exclusion, Enrollment, Randomization, and Follow-up

Can't see very well?

Make extra copies for your presentation!

(Ask us for assistance.)

Illustrate with most important parts



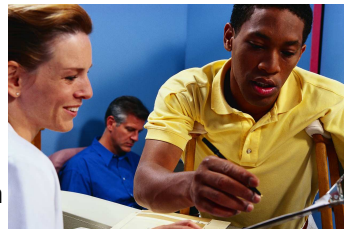
Methods: Subjects / Participants / Patient / Population

Inclusion criteria specific:

- 18+ yo, diagnosed LDH
- 6 weeks persistent symptoms 🇸🇨
- Pre-enrollment, non-operative treatment 🇸🇨 not specified
- All participants were surgical candidates 🇸🇨

Exclusion criteria:

- Prior surgery
- Cauda equina syndrome (CES)
- Other physical, mechanical conditions well-defined
- Unwilling / unable to have surgery within 6 months 🇸🇨



Baseline differences

- Did the population, experimental and control or comparison groups start with the same baseline demographics and prognostic factors?
 - Clinical trials
 - RCTs
 - Cohort
 - Case series
- How homogeneous is the population selected?
- **Confounders:** 2 or more factors that are “associated” (age and weight) and may affect (confuse, distort, augment?) the effect of the other factors on the outcome (onset of diabetes)

CONSORT definitions Consolidated Standards of Reporting Trials

<http://www.consort-statement.org/>

- *Selection bias* — a systematic error in creating intervention groups, causing them to differ with respect to prognosis. The groups differ in measured or unmeasured baseline characteristics because of the way in which participants were selected for the study or assigned to their study groups
 - Stratified severity of pain within a group versus mean similarity between group
- *Confounding* — a situation in which the estimated intervention effect is biased because of some difference between the comparison groups apart from the planned interventions such as baseline characteristics, prognostic factors, or concomitant interventions. For a factor to be a confounder, it must differ between the comparison groups and predict the outcome of interest
 - Pre-enrollment nonoperative care?

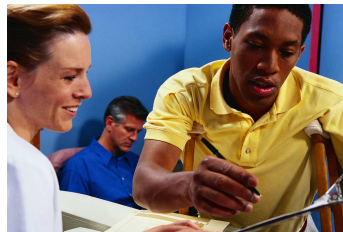
Methods: Subjects / Participants / Patient / Population

Baseline characteristics *between* groups similar:

- Mean age 42, gender, race, income, etc

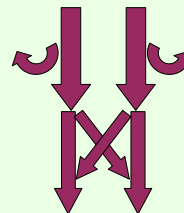
Baseline outcome scale measurements

- Similar between groups
- Within group no stratification 🏠
- 20% of baseline said symptoms were “getting better”
- Chosen or assigned to surgery?
- Initial bias toward surgery, surgery benefits?



Follow-up / Accountability

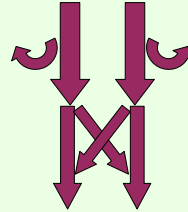
- Were all study participants or subjects accounted for at the end of the study?
- Rule-of thumb: >20% drop-out, non-adherence affects validity
- Unintended cross-over
- Cross-over not accounted for affects validity
- Are the reasons why patients withdraw from clinical trials included in the follow-up information?



Follow-up / Accountability

Intent to treat analysis

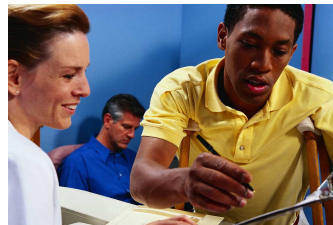
- include / analyze all patients in the group to which they were assigned
- regardless of whether or not they finished the study
- regardless of compliance
- High rate of crossover dilutes power of intervention



Methods: Subjects / Participants / Patient / Population

Follow-up / Accountability:

- 94% (472) completed at least one follow-up
 - Included in study data analysis
- Pre-determined follow-up periods: 6 weeks, 3, 6, 12, 24 mo
 - Missing data included in intent to treat analysis



Ethical Approval

- Institutional Review Board (IRB)
- Informed consent
- Disclosure of methods, intervention, risks, predicted benefits
- Different from affiliation and support



Methods: Intervention

- Describe intervention
 - Relate to PICO question
 - Described sufficiently so that the reader (practitioner) can adequately deliver the same intervention?
 - Adequate length in experimentation / observation / trial and measurement?
 - Adequate number of visits provided at appropriate intervals and frequency?
- With what was the investigated or experimental intervention compared?
 - Gold standard, alternate, placebo, sham?
- Describe Randomization
- Blinding

Methods: Intervention

Intervention

- Standard open discectomy well described
- Provided by experts, experienced surgeons
- Standardized and references provided
- Follow-up visits: 6 weeks, 3, 6, 12, 24 mo

Comparison

- Nonoperative treatments
 - Heterogeneous, not well controlled or determined 🇺🇸
 - Includes chiropractic, osteopathic, physical therapy, acupuncture, education, exercise therapy, NSAIDS and other meds, use of “devices” (shoe inserts to TENS)
 - Comparable to each other?
 - Comparable to surgery

Methods: Randomization

- Eligibility determined by nurse
- Randomized by computer upon enrollment
- Within sites
- Blind to enroller
- No other blinding possible due to nature of surgery and non-surgery
- All patients were candidates for surgery
- All patients were willing to undergo surgery if randomized to that group
- Data analysis blind to initial randomization, cross-over

Methods: Outcomes, measurement, observation

Outcome:

- What is actually measured
- Clinical event or accomplishment of interest, desired effect, end product or consequence following an intervention or exposure
- Clinically relevant
 - “a reduction in blood pressure,” “reduced mortality,” “better quality of life,” “management of blood glucose levels,” “resolution of pain,” etc.
- Biologic outcomes or surrogate endpoints (decrease in blood glucose levels, decrease in serum IgE levels, half-life of a drug in serum samples) may not singularly correlate with a clinical outcome (control of diabetes, death, recovery from a disease, decrease in blood pressure).
 - “Flaw” to make a “claim” regarding a clinical outcome when a biological outcome or surrogate endpoint is assessed
- “Outcomes” and results are different
 - measurement of an outcome is reported as a result.

Outcomes Measured

- Primary outcomes: changes from baseline bodily pain and physical function:
 - the Medical Outcomes Study (a 36-item Short-Form Health Survey scales)
 - the modified Oswestry Disability Index (American Academy of Orthopaedic Surgeons MODEMS version)
 - Measured at 6 weeks, 3 months, 6 months, 1 and 2 years from enrollment.
- Secondary outcomes:
 - sciatica severity (Sciatica Bothersomeness Index)
 - satisfaction of self-reported improvement of symptoms
 - employment status and quality of life function assessment

Results

- 1991 eligible
- 501 enrolled
- 472 (94%) completion (at least 1 follow-up)
- Data available 73-86% for patients at each follow-up
- Baseline characteristics similar (average of group) for both groups
- Non-adherence to treatment assignment affected both groups
 - 43% nonoperative treatment “crossed” to surgery
 - All patients enrolled were surgery candidates
 - Baseline
- Baseline characteristics for cross-over to surgery statistically different from non-crossover.

Results

Table 2. Nonoperative Treatments

| | No. (%) (n = 323)* |
|--|-----------------------|
| Clinicians/services | |
| Education/counseling | 392 (99) |
| Emergency department | 52 (16) |
| Surgeon | 119 (37) |
| Chiropractor | 95 (11) |
| Internist/neurologist/other physician | 195 (50) |
| Physical therapist | 142 (44) |
| Acupuncturist | 13 (4) |
| Injections | 103 (53) |
| Other | 102 (32) |
| Medications | |
| NSAIDs | 103 (50) |
| COX-2 inhibitors | 101 (31) |
| Oral steroids | 15 (5) |
| Narcotics | 147 (45) |
| Muscle relaxants | 65 (20) |
| Other | 172 (53) |
| Devices | |
| Brace | 10 (5) |
| Corset | 3 (3) |
| Migraine | 12 (4) |
| Orthopedic pillow | 30 (12) |
| Shoe inserts | 25 (8) |
| TENS device | 12 (4) |
| Other medical devices | 27 (8) |
| None | 216 (50) |

Abbreviations: COX-2, cyclooxygenase-2; NSAIDs, non-steroidal anti-inflammatory drugs; TENS, transcutaneous electrical nerve stimulation.

*Patients who had used clinicians, treatments, medications, and devices within 1 year following enrollment or until the time of surgery. 323 patients either had no surgery in the first year of enrollment or had at least 1 regularly scheduled follow-up prior to surgery at which non-operative treatment information could be assessed.

Results

- Both groups showed strong improvements at each follow-up time

Intention to treat analysis

- Primary outcome measures: non-statistically significant advantage for surgery
- Secondary outcome measures: favored surgery
 - None significant
 - Self rated progress $p = 0.04$ statistically significant for surgery

As treated analysis (based on treatment)

- Strong, statistically significant advantages for surgery

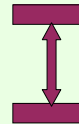
Statistical Analysis

“p value”

- Probability that any particular outcome would have arisen by chance.
- “Standard scientific practice” (often considered somewhat arbitrary):
 - $p < 0.05$ (p value less than one in twenty) is “statistically significant”
 - $p < 0.01$ (p value less than one in one hundred) is “statistically highly significant”
 - p values > 0.05 (e.g., 0.49, or 0.30) are not considered statistically significant
- Statistically significant: reject the “null hypothesis”;
 - p values in the non-significant range indicate that either there is not difference between groups OR there are too few subjects to demonstrate a difference (if a difference exists). It does not determine which circumstance the p value reflects.
 - Typically, “positive trials” show a statistically significant difference between groups or arms of a trial, and “negative trials” appear to show no significant difference between groups or arms.
- Statement of cutoff chosen for the study (e.g., $p < 0.05$ or $p < 0.01$)



Confidence Interval



- States an upper and lower limit (range or interval) and the likelihood that a certain percentage of results will fall between that interval.
- Defines the “% confidence” that the true value of a measurement or calculation lies within a certain range
- Allows the estimation for both positive trials (show a statistically significant difference between groups or arms of a trial) and negative trials (those which appear to show no significant difference) whether the strength of the evidence (results of outcomes measured) is strong or weak, and whether the study is definitive (precludes the need for further, similar or repeated studies).
- A typical clinically relevant confidence interval of 95%.
- The wider the confidence interval, the more likely that a certain result will fall within that interval. Strong evidence will have a wider confidence interval.



Statistical Analysis

- Sample size allowed up to 20% missing data
- Analyses for primary and secondary outcomes used all available data
- Predetermined outcomes
- Predetermined endpoint measurement times.
- Adjustments, analysis made for missing data
- $P < 0.05$ used to determine statistical significance
- Confidence intervals (CI) of 95% for mean treatment effects at each designated time
- Global tests of joint hypothesis of no treatment effect at any designated time performed

Validity & Limitations

- Representative population?
- Bias in selection, prognostic factors, confounding factors
- Follow-up: drop-outs threaten validity
- Ignoring withdrawals typically favors intervention
- Comparison should be equivalent
- Non-adherence (cross-over) threatens validity when $>20\%$
- “Intention-to-treat” analysis adjusts for drop-outs, not cross-over
- Dilution of effect of intervention (surgery)
- “As-treated” analysis may compensate for cross-over, but may exaggerate effect of intervention if unmeasured or differing baseline factors favor intervention

Validity & Limitations

- Hypothesis assumes intervention and comparison are equal
 - Objective: To assess the efficacy of standard open disectomy with involved nerve root examination
 - Null hypothesis: Surgery is not as effective as nonoperative treatments
 - Hypothetical results “either – or”
 - Cross-over rates do not support either - or
 - Typical consensus therapy not either - or
 - Surgical intervention is defined
 - Nonoperative treatments are heterogeneous
 - Surgery compared to multiple treatments, not necessarily a “gold standard” or single standard of care



Validity & Limitations

- Selection population not necessarily representative
 - Strict eligibility criteria may limit generalizability
 - Lack of surgery candidates agreeing to be randomized into surgery or nonoperative treatment?
 - All candidates for surgery
 - All agree to randomization to surgery or nonoperative care
- No blinding (“masking”) using sham surgical techniques due to practical and ethical constraints
- Pre-enrollment care not limited, considered
 - Many patients crossed over into the other treatment groups which could limit the benefits of randomization (protection against confounding factors coming into play and affecting outcome)



Validity & Limitations

- Baseline characteristics / eligibility favors surgery benefit (previous studies)
- High rate of non-adherence (crossover) affected both groups
 - 43% of nonoperative patients crossed over to surgery
 - Intention to treat analyzes results with initial group
 - Crossover to surgery with intention to treat analysis dilutes positive effect of surgery (favors nonoperative)
- Characteristics of cross over to surgery were statistically different: more baseline pain, disability, lower income
 - More prone to “need” surgery



Clinical Impact & Significance

- Do the studies add anything to the body of evidence?
- What is your evaluation of the strength of the evidence presented in these selected papers?
- Does your appraisal of the papers indicate studies are as strong as / stronger than the “CEBM” designations indicate?
- Is the evidence presented strong, moderately strong, neutral or weak if therapy, prognosis or etiology papers were selected?
- Does the evidence support the therapy, diagnosis, procedure or diagnostic tool discussed?
- What is the clinical significance in light of your patient?
- Form a “Clinical Impact Statement” referring to your patient

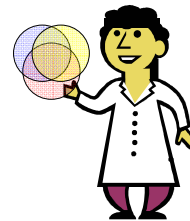
Clinical Impact & Significance

- Provides statistical evidence for considering nonoperative treatment as first option
 - Depending on location of herniation, age, time of onset
 - Results are consistent with clinical experience and consensus
- Intent-to-treat analysis with high cross-over make conclusions regarding superiority or equivalence of surgery compared to nonsurgical treatment limited to invalid for a generalized population
 - Patient specific, symptom specific

Clinical Impact & Significance

Impact statement:

Using this study and related articles from the SPORT trial, patients with LDH, bodily pain and disability may try conservative care unless the pain and disability are too much to bear. Further research on “reverse hypothesis” looking at specific conservative therapies compared to “standard,” efficacious surgical intervention should be done.



What's next?

- Review Forming a Clinical Question: PICO
- Review abstracts found last week.
- Select primary research article for Journal Club.
 - You may select review articles for background support only.
 - Other primary research articles may be used as additional resources.
 - JTASS and search strategy presentation lab next week
- Full text of the selected article due: 11/01/2007
 - Fill out "How I'll find it" form & hand in.
 - Review Accessing the literature resource in Section 3