

Therapy for Chronic Low Back Pain

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

JAMA[®]

The Journal of the American Medical Association

ABSTRACT LINK:

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

Type of study: Therapy

Study design: Randomized Controlled Trial

Presented by:

Barbara M. Sullivan, Ph.D., Dept. of Research, NUHS



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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?”

Back Pain Therapies: Patient Scenario



James 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.



Topic:

Clinical Question using the PICO format

	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...	to treat / relieve chronic (neck / back) pain (mild) depression
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:

Search Engines / Program(s) & Databases searched

- 1) Google, NBC5.com
- 2) Natural Standards (www.naturalstandards.com)
- 3) Entrez PubMed
- 4) EBSCOhost: CINAHL, AMED

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

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

Search strategy and results:

Limits and Special Techniques:

- Patient info; local TV channel website Google search back pain
- MeSH for “surgery” led to “nonoperative” term; 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

Full Query:

- ((low[All Fields] AND ("back"[MeSH Terms] OR back[Text Word])) OR (("lumbosacral region"[TIAB] NOT Medline[SB]) OR "lumbosacral region"[MeSH Terms] OR lumbar[Text Word]) OR ("spine"[MeSH Terms] OR spine[Text Word]) OR ("neck"[MeSH Terms] OR neck[Text Word])) AND (("surgery"[Subheading] OR "operative surgical procedures"[Text Word] OR "surgical procedures, operative"[MeSH Terms] OR "surgery"[MeSH Terms] OR surgery[Text Word]) AND nonoperative[All Fields] AND ("therapy"[Subheading] OR ("therapeutics"[TIAB] NOT Medline[SB]) OR "therapeutics"[MeSH Terms] OR treatment[Text Word]) AND ("pain"[MeSH Terms] OR pain[Text Word]))

Search strategy and results:

Link to Search Results (RSS):

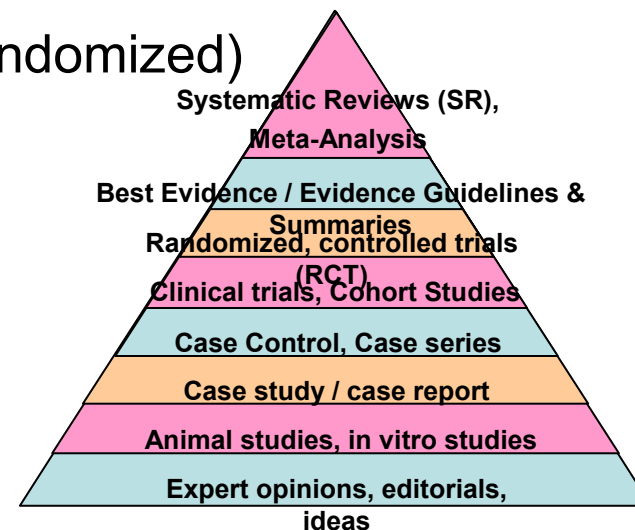
- http://eutils.ncbi.nlm.nih.gov/entrez/eutils/erss.cgi?rss_guid=0fxkB_HGVO9MNB3hbtrORXCI Zix0stFDdCT72jgyxEN

Full text accessed by:

- Free Full Text through JAMA publisher's link on PubMed
- Other associated JAMA articles available through NUHS LRC e-subscriptions

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
- Randomized trial
- Observational cohort (non-randomized)



Aims of Complete SPORT Study

Birkmeyer et al. Spine 2002;27:1361–1372.

- To simultaneously conduct three multicenter **randomized controlled trials comparing surgical and nonsurgical treatment** with repeated longitudinal measurement up to 24 months for patients considered eligible for surgery with
 - Intervertebral disk herniation (IDH)
 - Spinal Stenosis (SpS)
 - Degenerative Spondylolisthesis DS

- To **characterize subjects** declining participation in randomization but agree to be followed as part of an observational cohort. (**treatments, outcomes, costs**)

- To formally **estimate the cost-effectiveness of surgical versus nonsurgical interventions** for IDH, SpS, and DS through a synthesis of the results from the randomized controlled trial and the observational study cohorts.



Birkmeyer et al. Spine 2002;27(12):1361–1372.

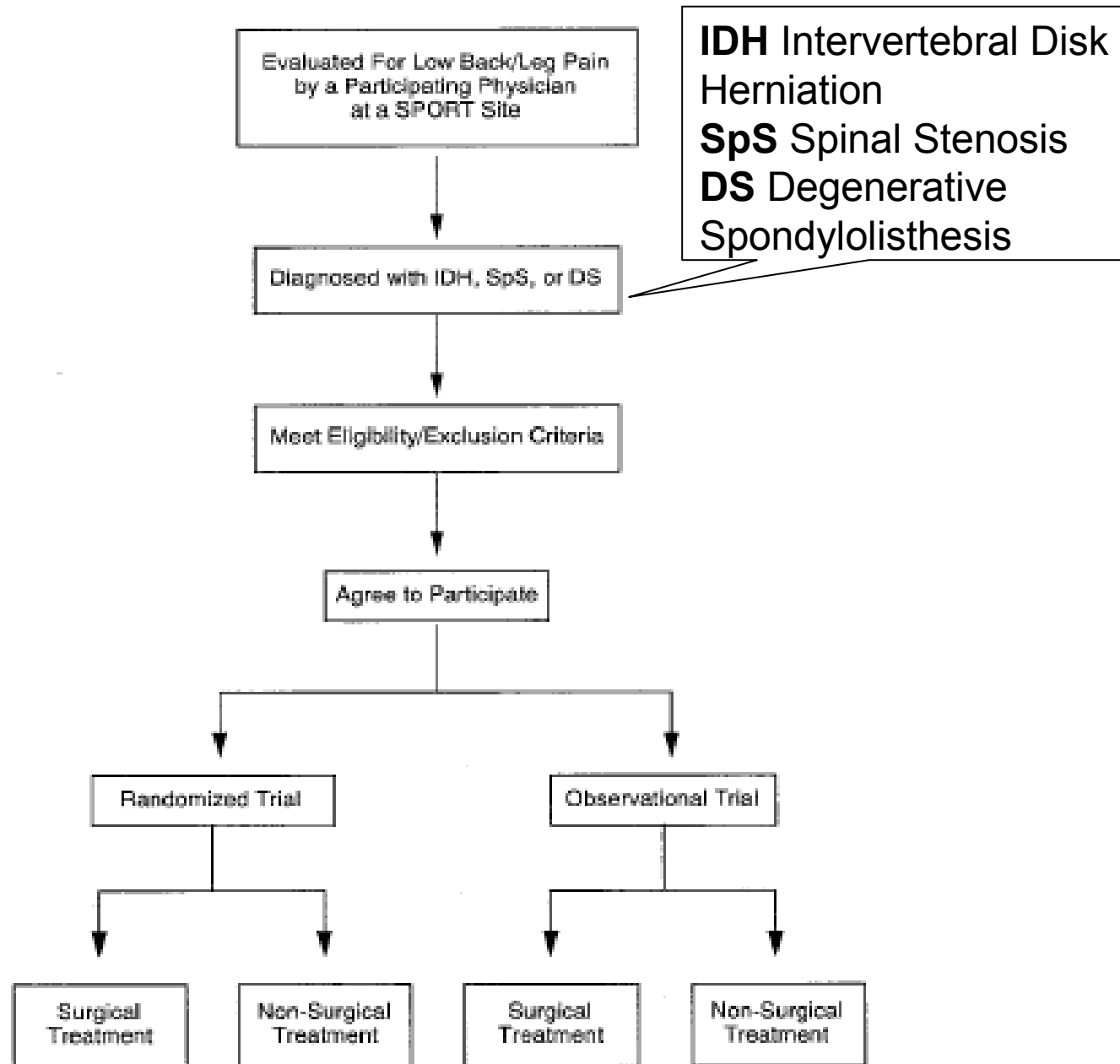


Figure 1. Overview of the SPORT study design.

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. [ABSTRACT](#)

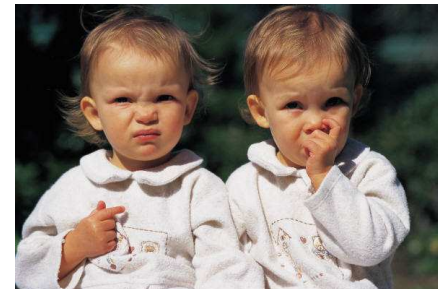
Study objectives and hypothesis

- Objective: To assess the efficacy of standard open diskectomy with involved nerve root examination *vs. nonoperative treatments*
- Lumbar Disk Herniation (LDH) and diskectomy
- Stated in abstract (modifications from SPINE paper)
- Hypothesis not clear 🏠
- Null hypothesis:
 - Surgery is not effective for lumbar disk herniation
 - Surgery is not as effective as nonoperative treatments 🏠
- Initial “intention to treat” analysis intent



Importance / Relevance / Context of the Research Question

- PICO: Is chiropractic manipulation / exercise / acupuncture as effective as surgery for relief of chronic low back pain?
 - Are nonoperative therapies effective for treating chronic low back pain in adults desiring alternatives to surgery?
- Research question: Is surgery effective (treatment) for lumbar disk herniation
 - 1^o outcomes: bodily pain, physical function, disability
 - 2^o outcomes: sciatica severity, satisfaction with symptoms, self-reported improvement, and employment status



Type of study, study design, strength

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



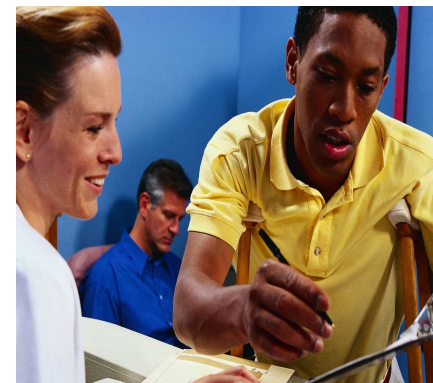
Ethical Approval

- Institutional subjects committee (each participating institution) approved standardized protocol
- All patients provided written informed consent
- Independent data and safety monitoring board monitored study at 6-month intervals



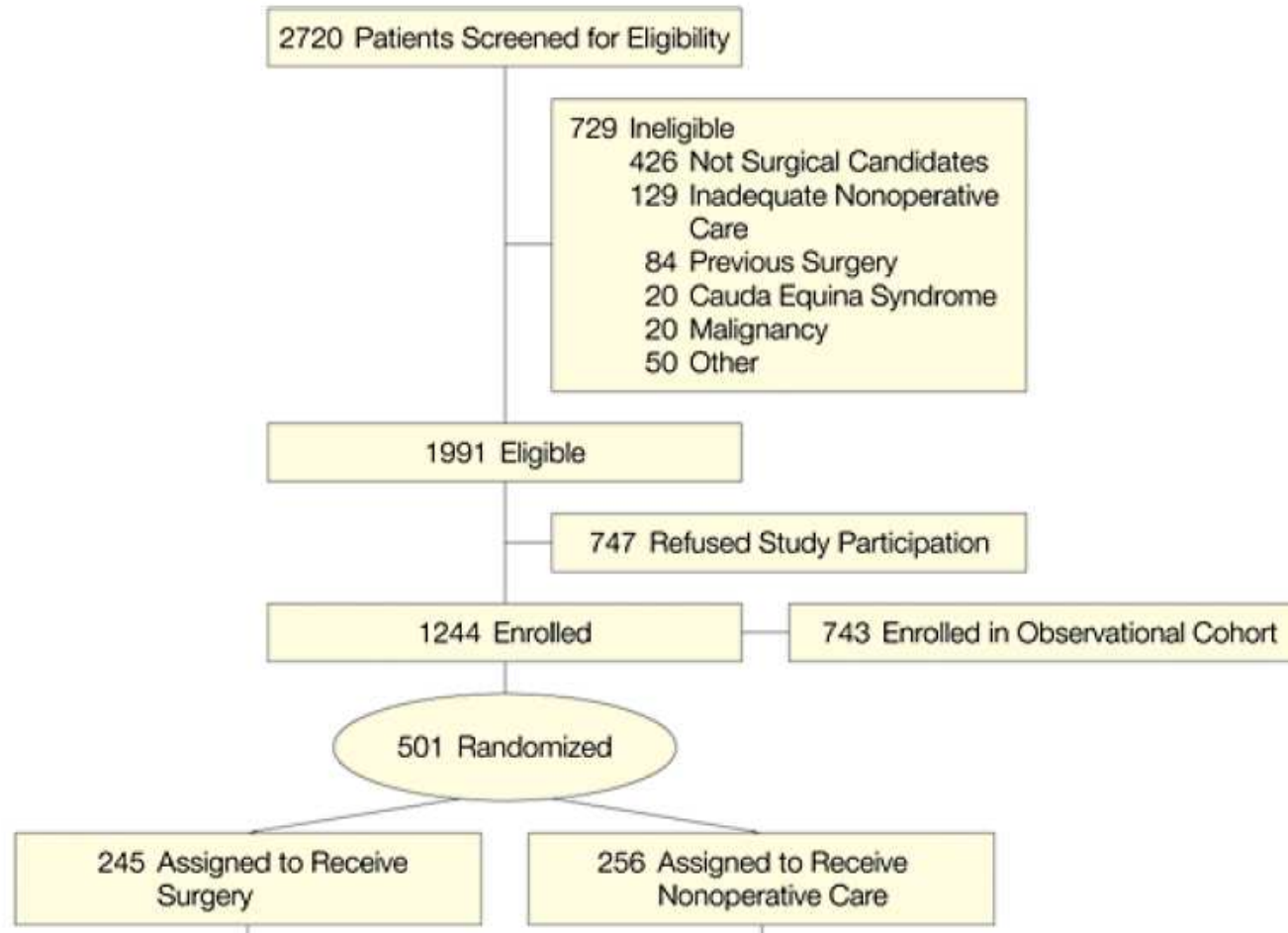
Methods: Subjects / Participants / Patient / Population

- Recruited from population presenting at 13 multidisciplinary spine clinics 🏢
- 11 states (US)
- 1991 eligible, 501 enrolled
- 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 🏢



Methods: Randomization

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



Weinstein, J. N. et al. *JAMA* 2006;296:2441-2450

<http://jama.ama-assn.org/cgi/content-nw/full/296/20/2441/JOC60155F1>

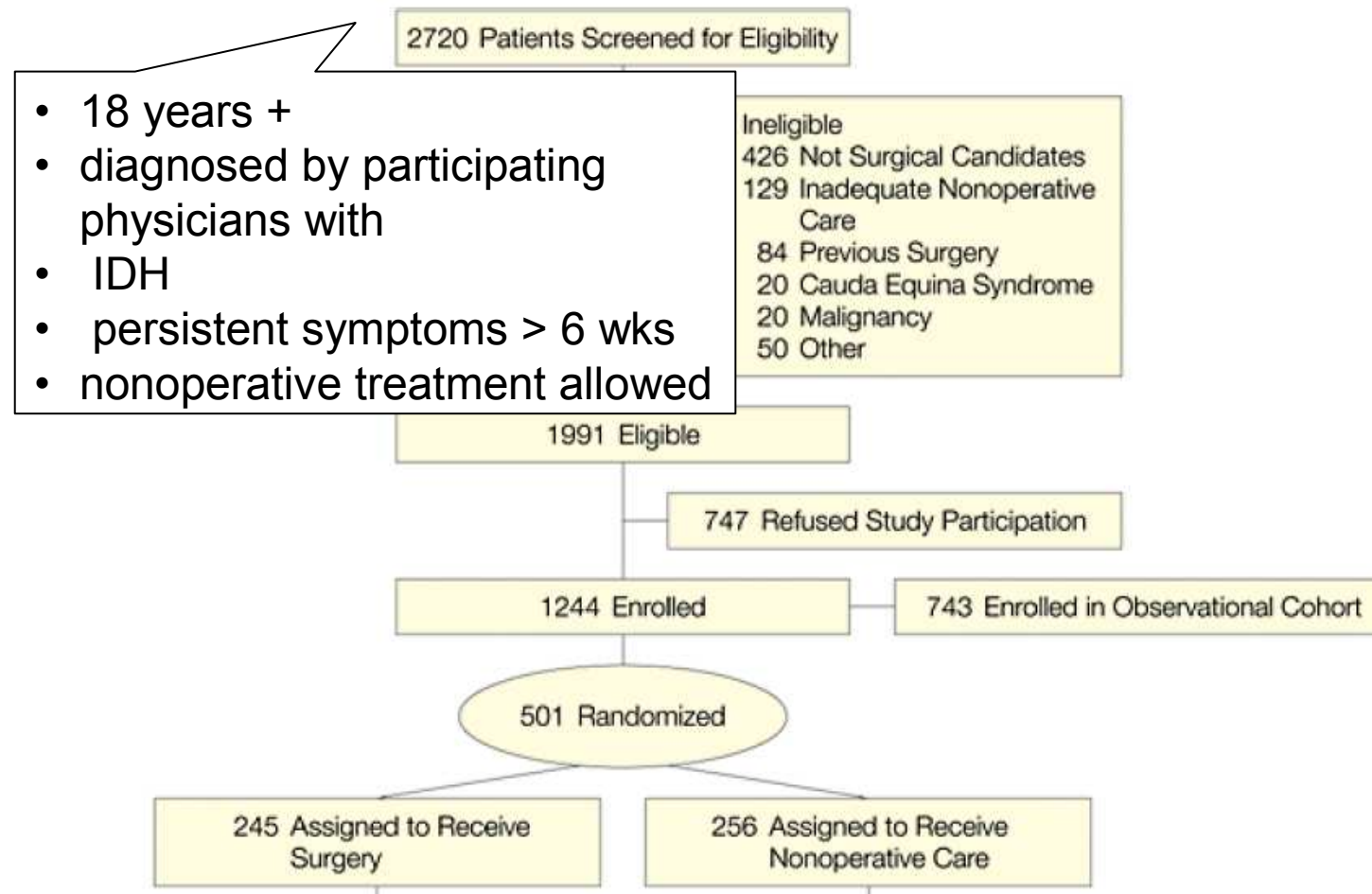


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Methods: Subjects / Participants / Patient / Population

Inclusion criteria specific:

- 18+ yo, diagnosed LDH
- 6 weeks persistent symptoms 🏠
- Pre-enrollment, non-operative treatment 🏠 not specified
- All participants were candidates for surgery 🏠

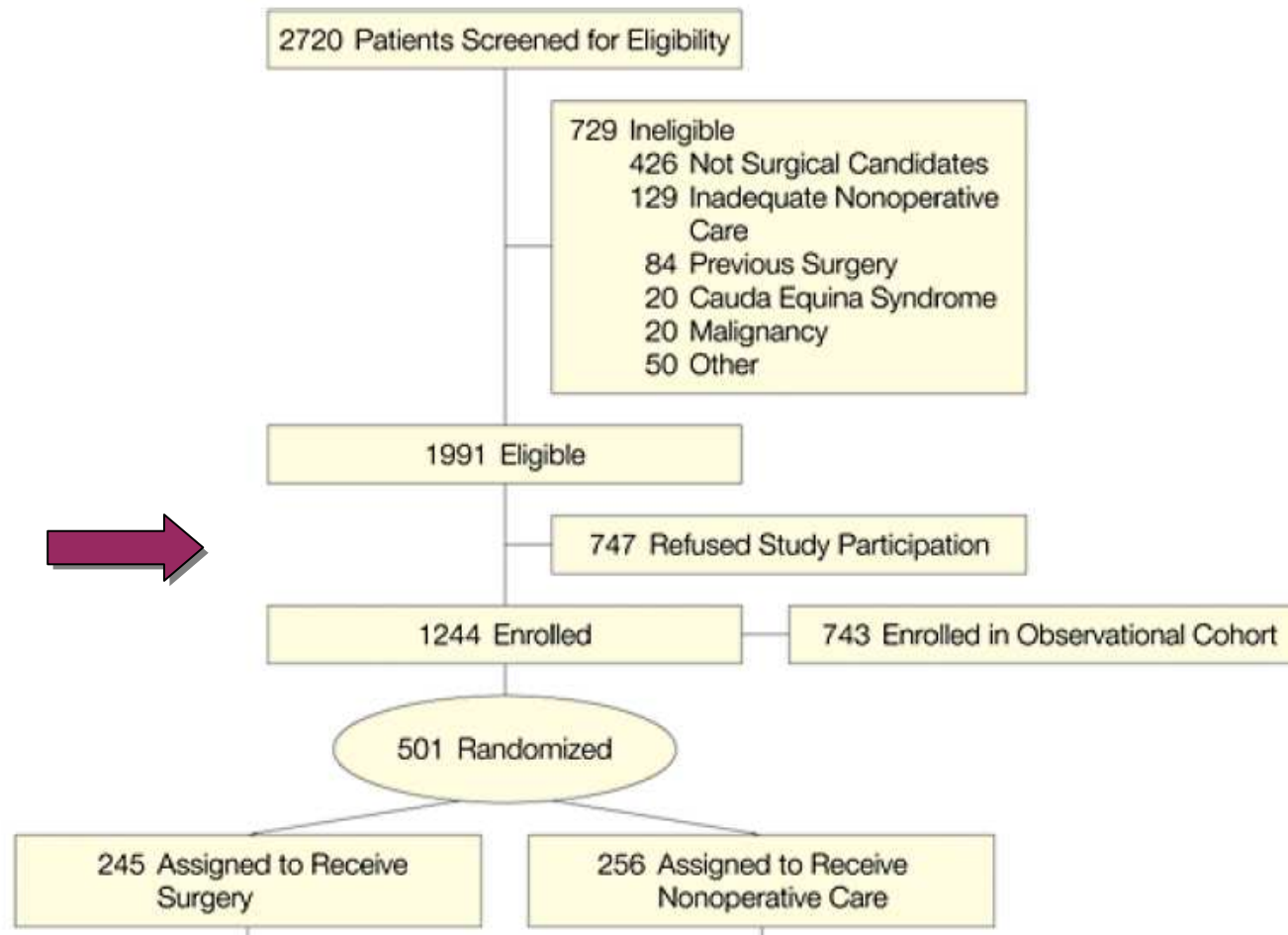
Exclusion criteria:

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



Methods: Randomization

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Methods: Blinding / Randomization

- Eligibility determined by nurse
- Diagnosed by participating physicians (disclosed)
- Randomized by computer upon enrollment
- Within sites
- Intervention group 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: 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?



Methods: Intervention

Intervention (245 / 501)

- 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 (256 / 501)

- Nonoperative treatments
 - Heterogeneous, not well “controlled” or defined 🏠
 - 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



Table 2. Nonoperative Treatments

	No. (%) (n = 323)*
Clinicians/services	
Education/counseling	299 (93)
Emergency department	52 (16)
Surgeon	119 (37)
Chiropractor	36 (11)
Internist/neurologist/other physician	195 (60)
Physical therapist	142 (44)
Acupuncturist	13 (4)
Injections	180 (56)
Other	102 (32)
Medications	
NSAIDs	193 (60)
COX-2 inhibitors	101 (31)
Oral steroids	15 (5)
Narcotics	147 (46)
Muscle relaxants	66 (20)
Other	172 (53)
Devices	
Brace	18 (6)
Corset	9 (3)
Magnets	12 (4)
Orthopedic pillow	38 (12)
Shoe inserts	25 (8)
TENS device	12 (4)
Other medical devices	27 (8)
None	216 (68)

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 visit prior to surgery at which nonoperative treatment information could be assessed.

Comparison: Nonoperative Treatment

- Initial groups:
 - 245 surgery
 - 256 nonoperative
- 323 had no surgery within 1st year
- Education 93%
 - CCGPP = A grade evidence is positive
- Clinician vs. specific therapy
- Multiple alternatives

**Weinstein, J. N. et al. JAMA
2006;296:2441-2450**

<http://jama.ama-assn.org/cgi/content-nw/full/296/20/2441/JOC60155T2>

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
- 247/251 underwent surgery in all (49.3%) within 2 years



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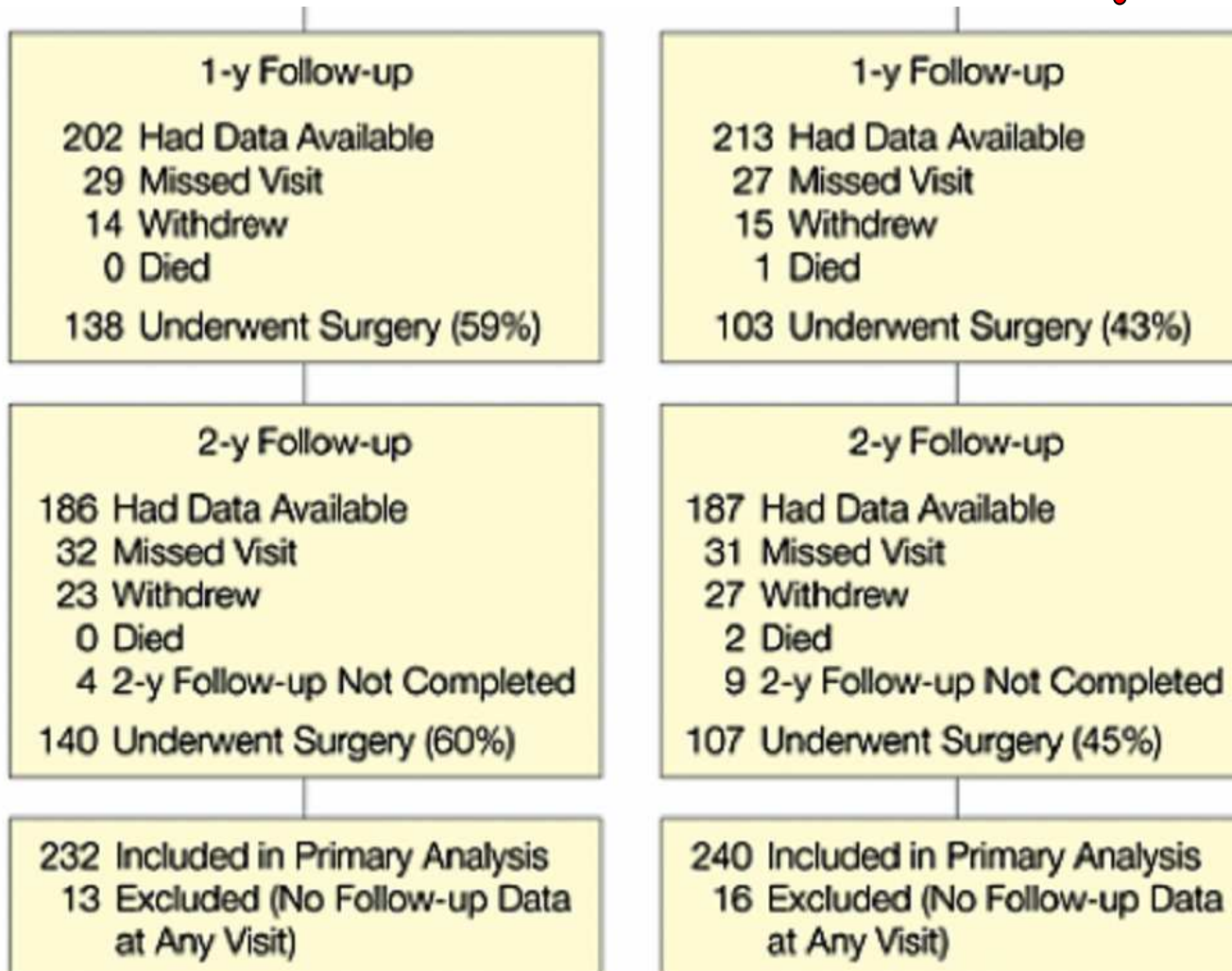
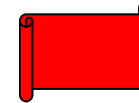
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Outcomes Measured

- 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







Outcomes Measured

- Outcomes are clinically relevant
- Outcome measurement tools are valid, well-recognized and referenced



Results

- 1991 eligible
- 501 enrolled in randomized, controlled trial
- 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

	3 Months		
	Surgery (n = 198)	Nonoperative (n = 211)	Treatment Effect (95% CI)
Primary outcomes			
SF-36 score, mean (SE)†			
Bodily pain	30.5 (1.9)	27.6 (1.8)	2.9 (-2.2 to 8.0)
Physical function	27.7 (1.9)	24.9 (1.9)	2.8 (-2.5 to 8.1)
Oswestry Disability Index, mean (SE)‡	-26 (1.7)	-21.3 (1.6)	-4.7 (-9.3 to -0.2)
Secondary outcomes			
Sciatica Bothersomeness Index, mean (SE)‡	-9.0 (0.46)	-6.8 (0.45)	-2.1 (-3.4 to -0.9)
Working full or part time, % (SE)	63.8 (3.3)	69.4 (3.1)	-5.6 (-14.5 to 3.4)
Satisfaction with symptoms: very/somewhat satisfied, % (SE)	54.3 (3.5)	43.0 (3.4)	11.3 (1.6 to 20.9)
Satisfaction with care: very/somewhat satisfied, % (SE)	86.8 (2.4)	83.3 (2.6)	3.5 (-3.3 to 10.3)
Self-rated progress since enrollment: major improvement, % (SE)	66.3 (3.3)	62.1 (3.4)	4.2 (-5.1 to 13.5)

Table 5. Treatment effects for Primary and Secondary Outcomes

Weinstein, J. N. et al. JAMA 2006;296:2441-2450

<http://jama.ama-assn.org/cgi/content-nw/full/296/20/2441/JOC60155F2>



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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



Results

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

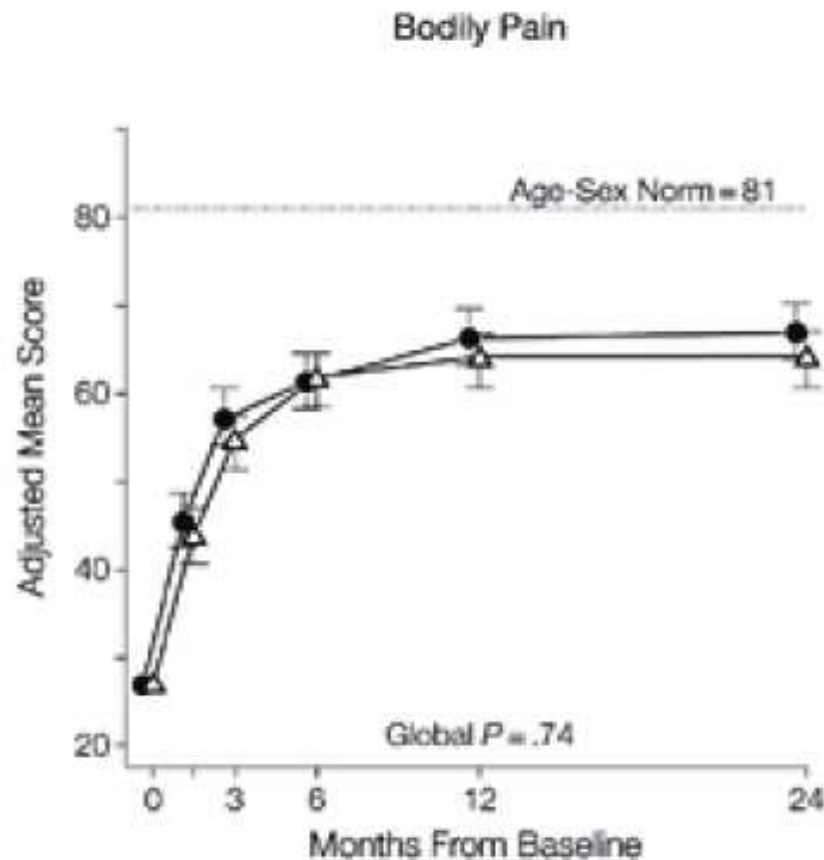


Figure 2. Mean Scores Over Time for SF-36 Bodily Pain
Weinstein, J. N. et al. JAMA 2006;296:2441-2450

<http://jama.ama-assn.org/cgi/content-nw/full/296/20/2441/JOC60155F2>



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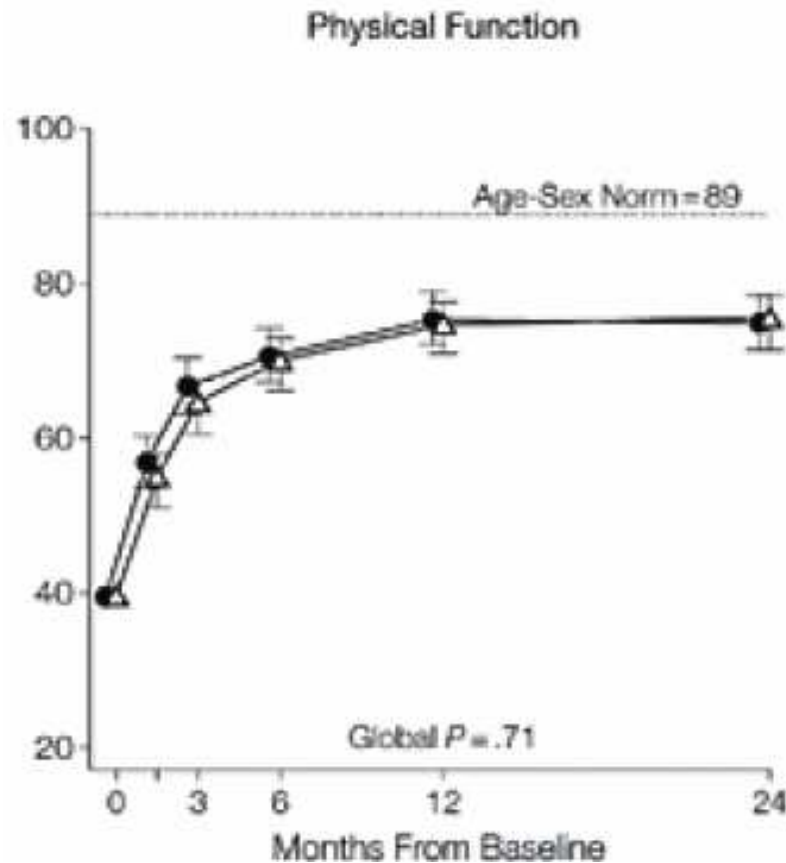


Figure 2. Mean Scores Over Time for SF-36 Physical Function Scale

Weinstein, J. N. et al. JAMA 2006;296:2441-2450
<http://jama.ama-assn.org/cgi/content-nw/full/296/20/2441/JOC60155F2>



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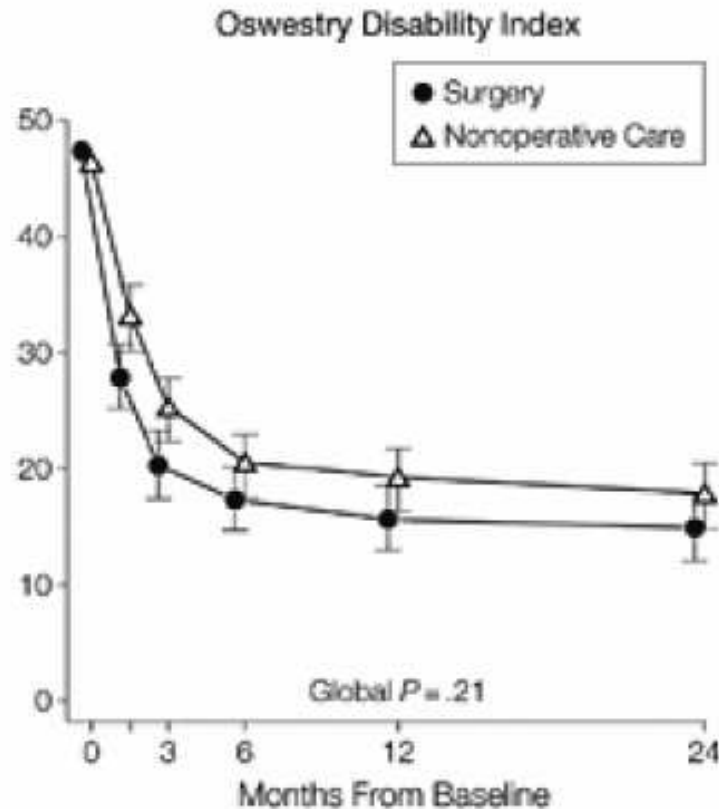


Figure 2. Mean Scores Over Time for SF-36 Oswestry Disability Index

Weinstein, J. N. et al. JAMA 2006;296:2441-2450

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Results

- Both groups showed strong improvements at each follow-up time
- For each outcome at each time point, treatment effect “favors surgery”
- BUT: treatment effects for 1^o effects
 - “were small
 - and not statistically significant at any of the points”

Table 5. Treatment effects for Primary and Secondary Outcomes

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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



Hypothesis / Research Question

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



Validity & Limitations

Population / Patient

- Selection population not necessarily representative
 - All candidates for surgery
 - All agree to randomization to surgery or nonoperative care for RCT
 - (rationale of cohort study)
 - Strict eligibility criteria may limit generalizability
 - Lack of surgery candidates agreeing to be randomized into surgery or nonoperative treatment?



Validity & Limitations

Population / Patient



- 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

Population / Patient



- Baseline characteristics / eligibility favors surgery benefit (previous studies)
- Characteristics of cross-overs to surgery were statistically different: more baseline pain, disability, lower income
 - More prone to “need” surgery
 - Possible confounding factors?



Validity & Limitations



Blinding

- Randomization blind to physicians diagnosing
- Randomization blind to enroller
- No blinding (“masking”) using sham surgical techniques due to practical and ethical constraints



Validity & Limitations

Follow-up / drop-out / cross-over



- 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)



Clinical Impact & Significance

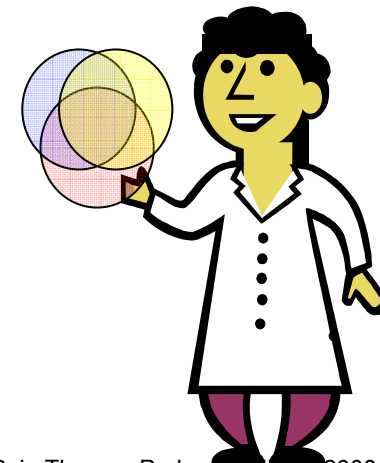
- Provides statistical evidence for considering nonoperative treatment as first option
 - Depending on location of herniation, age, time of onset
 - Results are consistent with clinical experience and consensus
- Intent-to-treat analysis with high cross-over makes conclusions regarding superiority or 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 nonoperative therapies compared to “standard,” efficacious surgical intervention should be done.



Discussion

- Potential bias or problems with the study
- Is this study valid?
- Did you see any flaws or bias with this study?
- Do you agree with the impact statement?
 - Why or Why Not?
- How would you treat / advise the patient?
- Do you feel this topic is applicable and important to the chiropractic profession?

