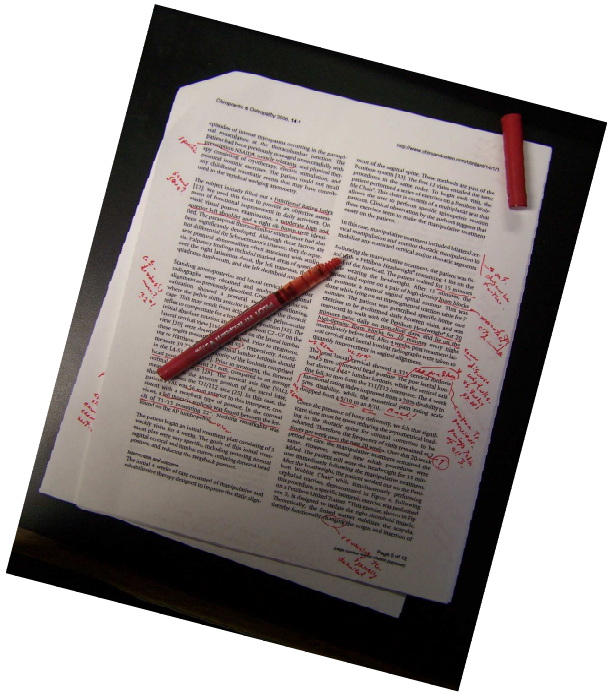
Journal Club Overview



- What is a “Journal Club?”
- Overview of the critical appraisal for primary research study designs
- Or, what are we doing now?

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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

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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

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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
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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.

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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
- Links practitioner to primary research
- Rapidly accessible, archived for your use in busy practices

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Critical Appraisals: EBP in Action

- *Several* critically appraised *primary research papers* focused on the same patient oriented clinical question = **C**ritically **A**ppraised **T**opic (**CAT**)
- *Several* summarized Critical Appraisals focused on the same topic = **B**est **E**vidence for a **T**opic (**BET**)

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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.acpjc.org/ available through NUHS EBSCOhost (search & browse)
  - Journal Review http://www.journalreview.org/

The Critical Appraisal

Let's look at a Critical Appraisal…

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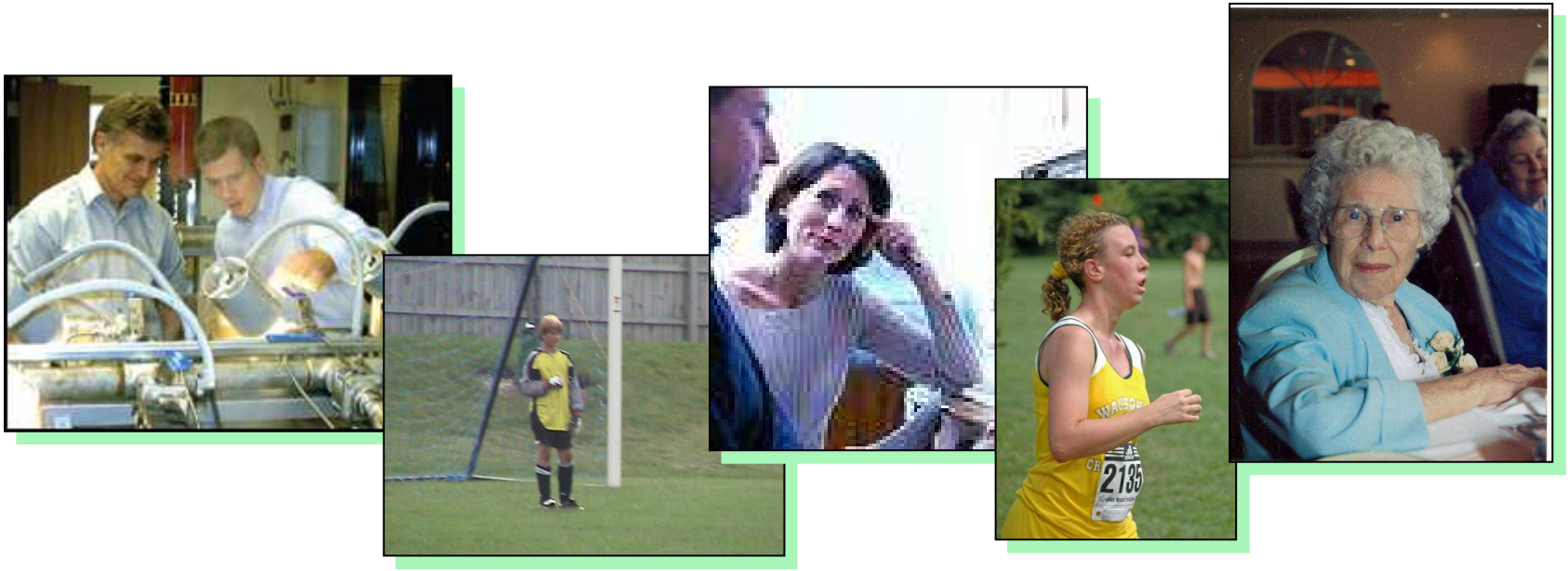
Back Pain Therapies: Patient Scenario

- 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)



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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?”

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]?			

Include the search strategy, results & evaluate:

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

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Search strategy and results:

Search Engines / Program(s) & Databases searched

1) Google, NBC5.com
2) Natural Standards (www.naturalstandards.com)
3) Entrez PubMed
4) EBSCO*host*: 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

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)

- Journal of the American Medical Association (JAMA) is peer reviewed, strong publishing history (1060), professional association AMA;
- Title key words focus on surgery versus non-operative for lumbar disc herniation;
- Authors have a publishing track record in spine research, surgery
- Large subject population from surgical centers is generalizable;
- Outcomes measured: pain (patient), physical disability; secondary sciatica, return to work, quality of life;
- 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®
The Journal of the American Medical Association

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

Type of study: Therapy

Study design: Randomized clinical trial

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

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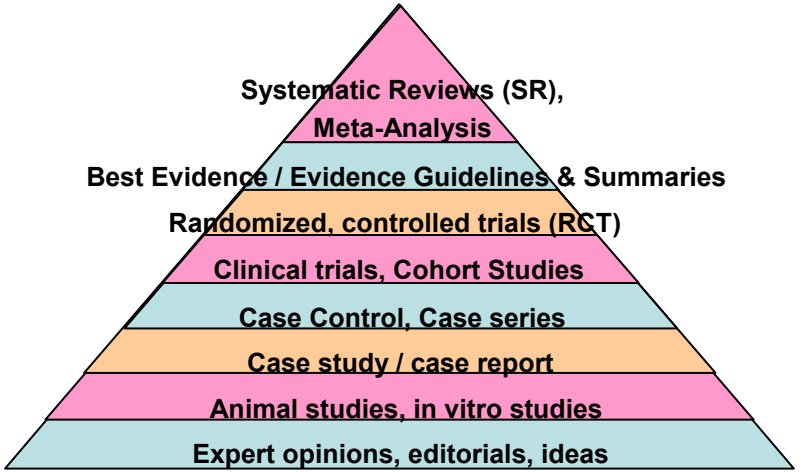
Study objectives and hypothesis

- 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 (RCTs)



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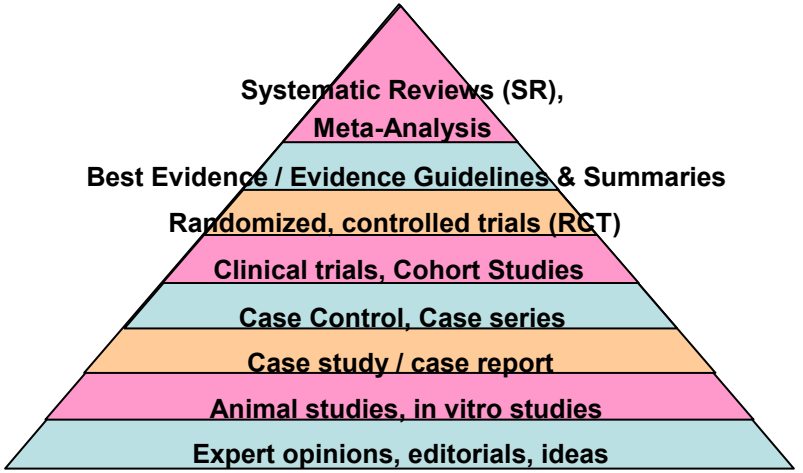
Type of study, study design, strength

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



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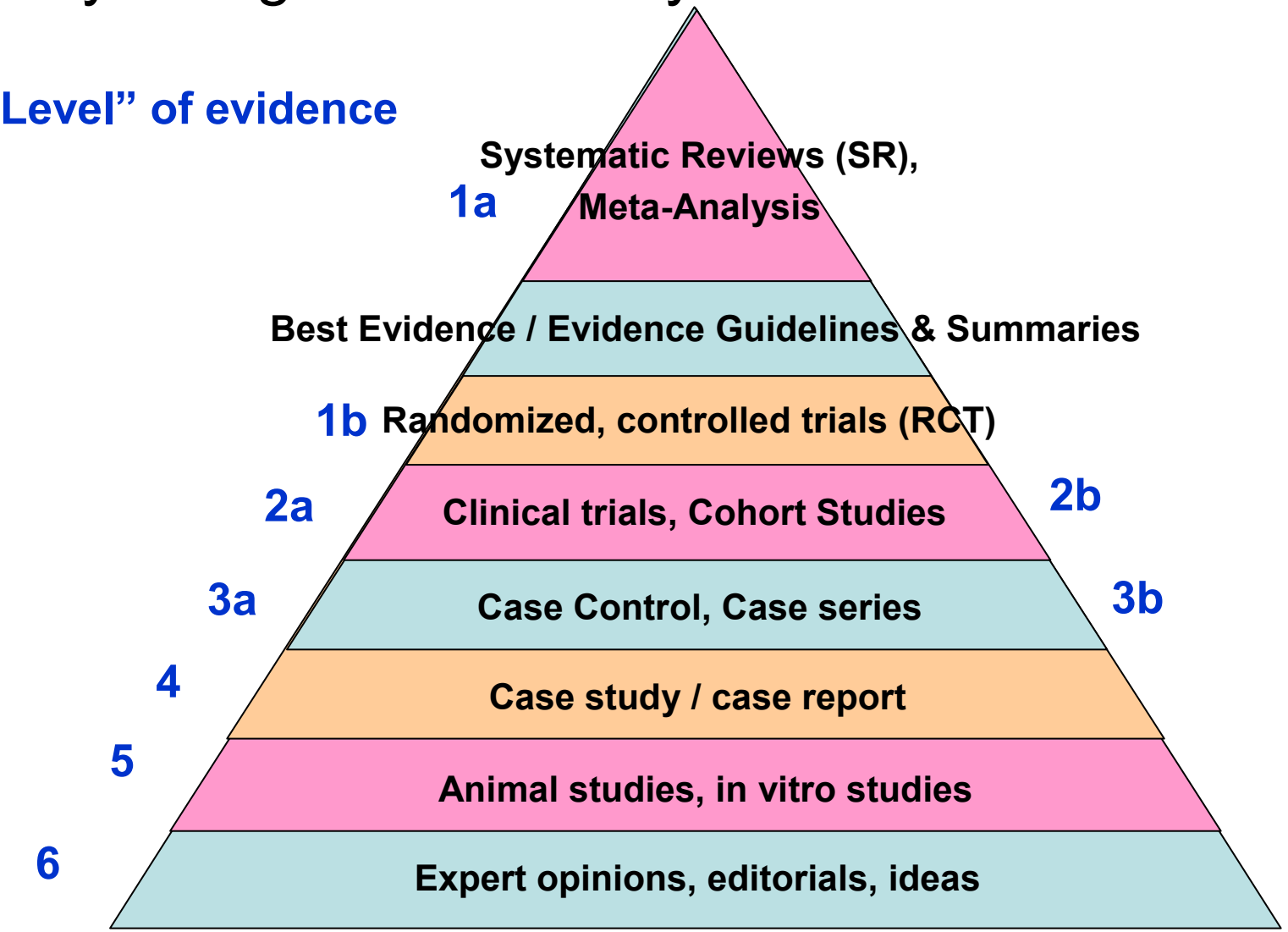
Study Design & “Hierarchy of Evidence”

“Level” of evidence



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“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:**

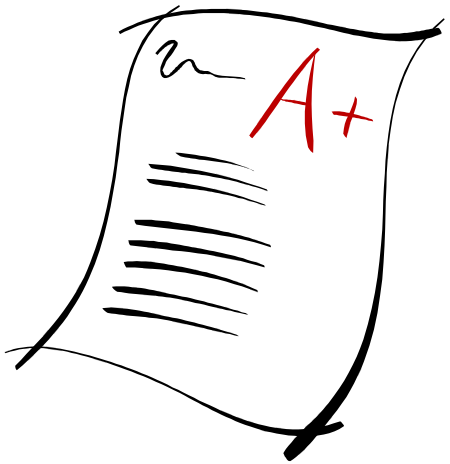
  cohort studies with untreated / exposed control, case control design,
  strong, well-defined case series

- **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



Methods: Subjects / Participants / Patient / Population

- Focus on PICO components,
  but don't leave out info that might affect validity
- "Real life" circumstances of study? (relevance)
- Population: large group of people (should be described)
- Sample: population subset selected from a larger population
- Selection population. Bias?
- Method of selection…
  - Why selected?
  - How were patients recruited? Bias?

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Methods: Subjects / Participants / Patient / Population

Selection bias:

- Differences in intervention and comparison groups due to
  incomplete randomization
  specific allocation
  decision of when a “case” is a “case”

Inclusion / exclusion criteria:

- Why subjects are enrolled in a study or left out
- Broad? Narrow? Generalizable?

Confounders:

- Characteristics or factors not under study or not included in criteria
- May affect the outcome of the intervention or disease

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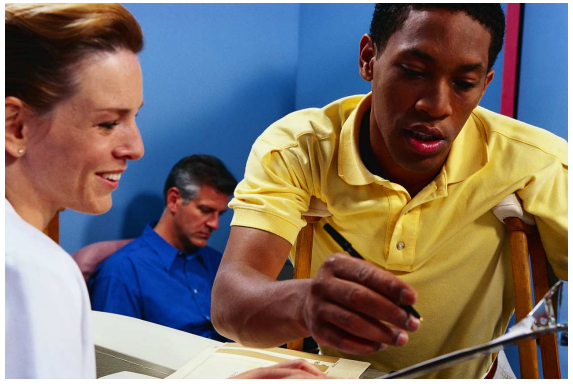
Methods: Subjects / Participants / Patient / Population

- Baseline differences?
  - Experimental and control groups start with similar prognosis
  - More homogeneity is stronger
- Did the population, experimental and control or comparison groups start with the same baseline demographics and prognostic factors?
- How homogeneous is the population selected?



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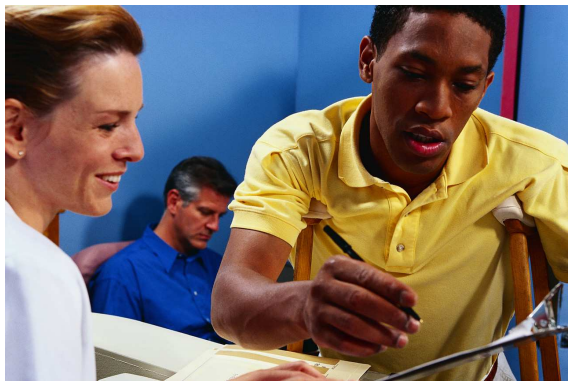
Methods: Subjects / Participants / Patient / Population

- Baseline differences?

- **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)



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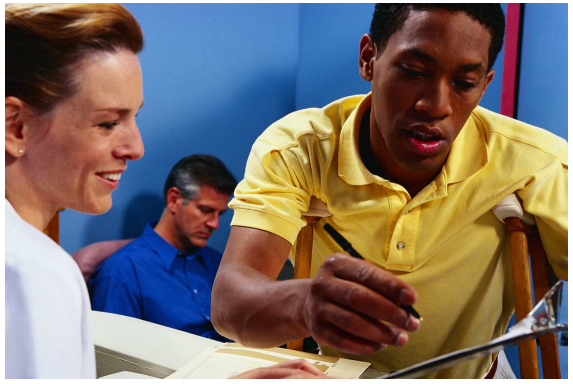
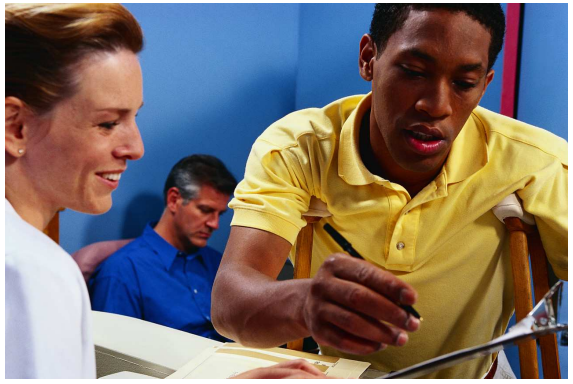
Methods: Subjects / Participants / Patient / Population

- Sample size adequate to support measurement of outcomes?
  - Rare event?
  - Likelihood of staying in the study, following through?
  - Size based on previous studies, outcomes?
  - Rationale for choosing sample size?



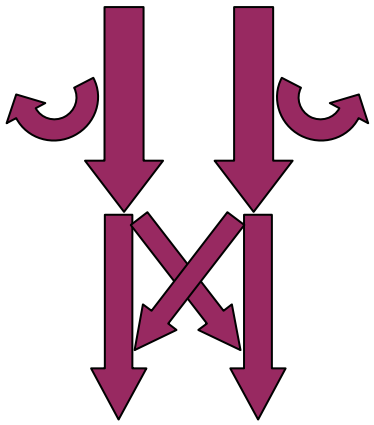
Methods: Subjects / Participants / Patient / Population

- Sample size adequate to analyze statistically?
  - Rule of thumb:
    30 subjects per group
  - Case series: at least 10 subjects with well defined characteristics, baseline, histories
  - Likelihood of staying in the study, following through?
  - Rationale for choosing sample size?



Follow-up / Accountability

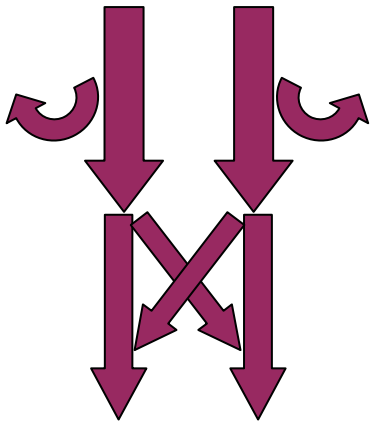
- Were all study participants or subjects accounted for at the end of the study?
- Rule-of thumb: >20% drop-out, non-adherence affects validity
- Unintended cross-over
- Cross-over not accounted for affects validity
- Are the reasons why patients withdraw from clinical trials included in the follow-up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



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
- Accounts for drop-out, not necessarily crossover
- High rate of crossover
  dilutes power of intervention



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?
  - Was the comparison valid? Realistic?
  - Why was the comparison selected?

Methods: Intervention

- Performance Bias
  - Difference in care provided to intervention and comparison groups case versus non-case or control
  - Other than difference in intervention / comparison
  - Population presenting at hospital versus control presenting at private practice
  - Systematic

Methods: Randomization

- Incomplete randomization and crossover threatens validity
- By computer upon enrollment
- By lottery / blind drawing
- No involvement of study investigator, recruiter, enroller, etc.
- Allocation to a particular group: cohort study
- Patient choice, provider's choice, expertise

Methods: Blinding

- Multiple points where investigators and subjects don't know…
- Provider determining eligibility does not know to what group a subject is randomized
- Subjects are blind to whether they receive treatment or comparison (placebo, sham, conventional treatment)
- Person providing treatment, dispensing does not know what they are providing (experimental, real, sham)
- Assessors are blind to randomized group, treatment, exposure, whether "case" or "control"

Methods: Outcomes, measurement, observation

Outcome:

- "Outcomes" and results are different
- Outcome: what is accomplished; what is 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
- Result: measurement of an outcome is reported as a result

Methods: Outcomes, measurement, observation

Outcome:

- 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
- Watch for validation of quantitative biological endpoint with accepted, subjective, qualitative, clinical outcome endpoint or measurement tool

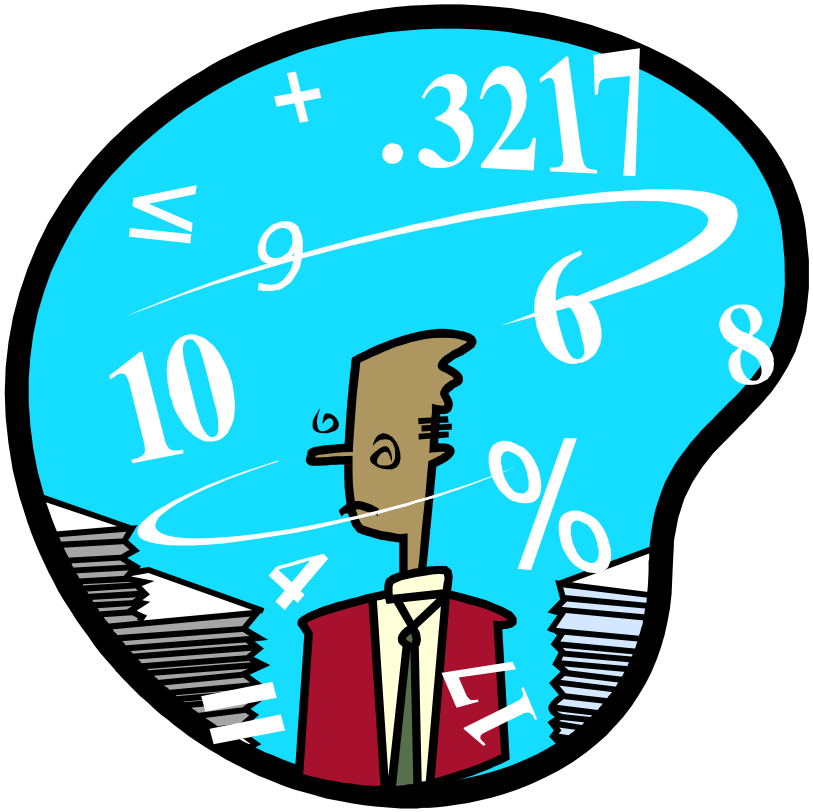
Outcomes Measured

- 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: calculation of measurement

- Primary outcomes: changes from baseline bodily pain and physical function
- Results:
  - Pain decreased in intervention group 72%
  - Disability index score decreased from 12 to 4
  - Pain measured by Visual Analogue Scale decreased in sham by 35%

Statistical Analysis



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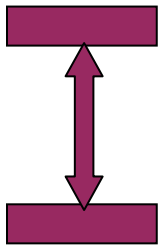
“p value”

- 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

“p value”

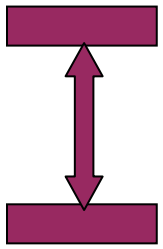
- Statistically significant: reject the “null hypothesis”
  - p values in the non-significant range indicate that either
    there is not difference between groups
    OR
    there are too few subjects to demonstrate a difference (if a difference exists).
  - Does not determine which circumstance the 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.
- Look for statement of cutoff chosen for the study (e.g., $p < 0.05$ or $p < 0.01$) and why

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.

Confidence Interval



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- 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 withdrawls typically favors intervention
- Comparison should be equivalent
- Non-adherence (cross-over) threatens vailidity 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

	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

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

Impact statement:

Using this study and related articles from the SPORT trial, patients with LDH, bodily pain and disability may try conservative care and expect reduction in pain and a return of physical function similar to the described surgical intervention, 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.