

Appendix 1. Evidence-based Medicine Systematic Literature Review

Title of Manuscript: _____

Authors of Manuscript: _____

Journal and Citation: _____

Identify and State the Hypothesis

Primary Hypothesis: _____

Secondary Hypothesis: _____

Type of Study:

Treatment Study Diagnosis Study Screening Study Prognosis Study Risk Factor Study

Study Design:

Randomized Controlled Trial Non-randomized Controlled Trial Cohort Study Case Control Study

Cross Sectional Study Case Series/Case Report

Methods:

Is there a Control or Comparison Group in the Treatment Study? Yes No

List Other Known Factors Not Controlled between the Groups: _____

Is the Study: Prospective or Retrospective?

Did the Author Control for Major Known Variables that Could Introduce Bias? Yes No

For a Diagnostic Study, What is the Gold Standard for Comparison: _____

Insert number (n) POPULATION	Allocation of Study Population			IS THERE A SOURCE OF BIAS?
	Group	Group	Group	
	↓	↓	↓	Selection Bias: <input type="checkbox"/> Yes <input type="checkbox"/> No
INTERVENTION	↓	↓	↓	List: • •
FOLLOWUP				Measurement Bias: <input type="checkbox"/> Yes <input type="checkbox"/> No
Initial	_____	_____	_____	•
Final	_____	_____	_____	Confounding ; <input type="checkbox"/> Yes <input type="checkbox"/> No
	%	%	%	•
OUTCOMES:				•
1°	_____	_____	_____	Independent Examiners: <input type="checkbox"/> Yes <input type="checkbox"/> No
2°	_____	_____	_____	Validated Questionnaire: <input type="checkbox"/> Yes <input type="checkbox"/> No
3°	_____	_____	_____	

Length of Reported Follow-up: Minimal _____, Average _____

If a clinical trial, were the study groups comparable at baseline (e.g. Age, Gender, Race, etc)? Yes No

Was Post-Treatment Care Similar (e.g. Rehabilitation Protocols) In Compared Groups? Yes No

Statistical Analysis

Were appropriate statistical methods used (e.g. type of test, estimator or confidence interval; choice of paired vs unpaired assessment; adjustment for baseline variables)?

- Yes, and methods required minimal assumptions.
- Yes, distributional (normal or non-normal) and other assumptions were justified.
- Probably; methods are appropriate in general for the type of response variable, but assumptions were not justified.
- No, but the test used is unlikely to affect the conclusions.
- No, and there is a good possibility that the inappropriate statistical methods used have affected the conclusions.

Is Statistical Consultation Requested? Yes No Who should do it? _____

Results

COMPARISONS OUTCOME/RESULT	ABSOLUTE DIFFERENCE Point Estimate + Confidence Limits	P-VALUE	IF NOT SIGNIFICANT, POWER = () FOR () DIFFERENCE, OR NARROW ENOUGH CONFIDENCE LIMITS?	IS DIFFERENCE CLINICALLY IMPORTANT?
				<input type="checkbox"/> Yes <input type="checkbox"/> No
				<input type="checkbox"/> Yes <input type="checkbox"/> No
				<input type="checkbox"/> Yes <input type="checkbox"/> No
				<input type="checkbox"/> Yes <input type="checkbox"/> No
				<input type="checkbox"/> Yes <input type="checkbox"/> No
				<input type="checkbox"/> Yes <input type="checkbox"/> No
				<input type="checkbox"/> Yes <input type="checkbox"/> No
				<input type="checkbox"/> Yes <input type="checkbox"/> No

Level of Evidence

- Level I Level II Level III Level IV Level V

Summary

Yes No Is there a comparison group in a TREATMENT STUDY? If No, then read for INFORMATION ONLY-THERE IS NO EVIDENCE-BASED REASON OR DATA TO CHANGE YOUR PRACTICE.

Yes No Are the groups compared and equivalent before treatment? If No, then RESULTS MAY NOT BE CAUSED BY THE TREATMENT, BUT BY THE PRE-EXISTING DIFFERENCES IN THE GROUPS.

Yes No Is the study free from a selection bias, either through original enrollment or through problems with follow-up? If No, THE IMPACT OF THE POTENTIAL SELECTION BIAS MUST BE ESTIMATED TO DETERMINE WHETHER THE RESULTS OF THE STUDY HAVE RELEVANCE.

Yes No Is the study free of a measurement bias? If No, THE STUDY RESULTS MAY BE MISLEADING DUE TO MISCLASSIFICATION OF STUDY SUBJECTS THROUGH INACCURATE MEASUREMENT.

Yes No Is the statistical analysis acceptable? Has potential confounding been addressed? Are the statistically significant findings clinically significant?

Yes No Does the study population reflect your practice population?

Yes No Do you have adequate training or experience to perform the treatment/technique and expect similar results?

If the answers to these questions are Yes, STRONGLY CONSIDER CHANGING YOUR PRACTICE!

REFERENCE MATERIALS FOR THE EVIDENCE-BASED MEDICINE SYSTEMATIC LITERATURE REVIEW

<u>1° Hypothesis or Topic Research</u>	<u>[Examples]</u>	<u>Preferred Research Design</u>
Treatment	[drug, prevention, surgery]	Randomized Controlled Trial
Diagnosis	[diagnostic test]	Cross-sectional Survey
Screening	[value of test]	Cross-sectional Survey
Prognosis	[disease, injury, condition]	Longitudinal Cohort
Risk Factor	[exposure to....]	Cohort or Case-Control

STUDY DESIGN TYPES – Characteristics LISTED IN HIERARCHY OF EVIDENCE

1. Randomized Controlled Trial – Only those randomized by computer or random number table are acceptable.
2. Cohort – Two or more groups selected basis differences exposure to “agent” and follow up.
3. Case Control-Patients with a particular disease/condition are matched to a control group
4. Cross-Sectional – Data is collected at a single point in time.
5. Case Reports/Case Series – Medical histories in one or more patients with condition or treatment.

LEVELS OF EVIDENCE FOR PRIMARY RESEARCH QUESTION				
	Types of Studies			
	Therapeutic Studies— Investigating the Results of Treatment	Prognostic Studies— Investigating the Outcome of Disease	Diagnostic Studies—Investigating a Diagnostic Test	Economic and Decision Analyses—Developing an Economic or Decision Model
Level I	1. Randomized controlled trial a. Significant difference b. No significant difference but narrow confidence intervals 2. Systematic review ² of Level-I randomized controlled trials (studies were homogeneous)	1. Prospective study ¹ 2. Systematic review ² of Level-I studies	1. Testing of previously developed diagnostic criteria in series of consecutive patients (with universally applied reference "gold" standard) 2. Systematic review ² of Level-I studies	1. Clinically sensible costs and alternatives; values obtained from many studies; multiway sensitivity analyses 2. Systematic review ² of Level-I studies
Level II	1. Prospective cohort study ³ 2. Poor-quality randomized controlled trial (e.g., <80% follow-up) 3. Systematic review ² a. Level-II studies b. Nonhomogeneous Level-I studies	1. Retrospective study ⁴ 2. Study of untreated controls from a previous randomized controlled trial 3. Systematic review ² of Level-II studies	1. Development of diagnostic criteria on basis of consecutive patients (with universally applied reference "gold" standard) 2. Systematic review ² of Level-II studies	1. Clinically sensible costs and alternatives; values obtained from limited studies; multiway sensitivity analyses 2. Systematic review ² of Level-II studies
Level III	1. Case-control study ⁵ 2. Retrospective cohort study ⁴ 3. Systematic review ² of Level-III studies		1. Study of nonconsecutive patients (no consistently applied reference "gold" standard) 2. Systematic review ² of Level-III studies	1. Limited alternatives and costs; poor estimates 2. Systematic review ² of Level-III studies
Level IV	Case series (no, or historical, control group)	Case series	1. Case-control study 2. Poor reference standard	No sensitivity analyses
Level V	Expert opinion	Expert opinion	Expert opinion	Expert opinion
<ol style="list-style-type: none"> 1. All patients were enrolled at the same point in their disease course (inception cohort) with greater than or equal to 80% follow-up of enrolled patients. 2. A study of results from two or more previous studies. 3. Patients were compared with a control group of patients treated at the same time and institution. 4. The study was initiated after treatment was performed. 5. Patients with a particular outcome ("cases" with, for example, a failed total arthroplasty) were compared with those who did not have the outcome ("controls" with, for example, a total hip arthroplasty that did not fail). 				

PROSPECTIVE VS. RETROSPECTIVE

In a Prospective Study, the study question and the data to be collected are determined before the study begins.

In a Retrospective Study, the study question is determined after the data has been collected. (Even if that data is general data collected in a prospective fashion). Prospective studies are better at getting the appropriate data to answer the question and are better at controlling the confounding variables.

BIAS

1. Selection Bias – Difference in comparison groups secondary to incomplete or insufficient randomization.
2. Performance Bias – Differences in care provided due to sources other than the intervention being evaluated.
3. Exclusion or Transfer Bias – Differences in groups that occur as a result of patients withdrawing from the trial.
4. Detection Bias – Different evaluations for outcomes best independent examiner or blinding examiner or validated outcome questionnaire self-administered.

STATISTICS

DATA CHARACTERISTICS	PARAMETRIC TEST	NONPARAMETRIC TEST
• Two independent samples from the same population	Two sample (unpaired) t-test	Wilcoxon-Mann-Whitney Test
• Two sets of observation from a single population	One sample (paired) t-test	Wilcoxon Signed Rank test
• Three or more samples from a single population	One-way analysis of variance (F)	Kruskal-Wallis test
• As above but tests influence (and interaction) of two different factors	Two-way analysis of variance	Two-way rank test
• Test null hypothesis that proportions of variables estimated from two or more independent samples are same	Chi-squared test (X^2 test)	Chi-squared test (X^2 test)
• Assesses strength of association between two continuous variables	Pearson's r Product moment Correlation coefficient	Spearman 's rank correlation coefficient
• Numerical relationship between two quantitative variables, allowing one value to be predicted from the other or Numerical relationship between a dependent variable and several predictor variables (co-variables)	Multiple regression by least squares method	Semiparametric regression (proportional odds, Cox proportional hazards model)