Therapy

Single Trials

- 1. Is this evidence about therapy (from an individual randomized trial) valid?
 - a. Was there a fair start?
 - i. Was the assignment of patients to treatment randomized?
 - ii. Was the randomization concealed?
 - iii. Were the groups similar at the start of the trial?
 - b. Was there a fair race?
 - i. Was follow-up of patients sufficiently long and complete?
 - ii. Were all patients analyzed in the groups to which they were analyzed?
 - c. Some finer points?
 - i. Who was blinded: Were patients, clinicians, and study personnel kept blind to treatment?
 - ii. Were groups treated equally, apart from the experimental therapy?
- 2. Is this valid evidence about therapy (from an individual randomized trial) important?
 - a. What is the magnitude of the treatment effect?
 - b. How precise is the estimate of the treatment effect?
 - i. RRR = |CER EER|/CER
 - ii. ARR = |CER EER|
 - iii. NNT = 1/ARR
- 3. Can we apply this valid, important evidence about therapy in caring for our patient?
 - a. Is our patient so different from those in the study that its results cannot apply?
 - b. Is the treatment feasible in our setting?
 - c. What are our patient's potential benefits and harms from the therapy?
 - d. What are our patient's values and expectations for both the outcome we are trying to prevent and the treatment we are offering?

Guides for whether to believe apparent qualitative differences in the efficacy of therapy in some subgroups of patients

- 1. A qualitative difference in treatment efficacy among sub-groups is likely only when all the following questions can be answered "yes":
 - a. Does it really make biological and clinical sense?
 - b. Is the qualitative difference both clinically (beneficial for some but useless or harmful for others) and statistically significant?
 - c. Was it hypothesized before the study began (rather than the product of dredging the data)?

- d. Was it one of just a few subgroup analyses carried out in the study?
- e. Is this subgroup difference suggested by comparisons within rather than between studies?
- f. Has the result been confirmed in other independent studies?
- 2. The likelihood of help vs. harm (LHH)
 - a. In applying a systematic review or RCT to an individual patient, we need to consider:
 - i. Our patient's risk, relative to patients in the trial, of the event we hope to prevent with the treatment: f_t
 - ii. Our patient's risk, relative to the patients in the trial, of the side-effect we might cause from the treatment: f_h
 - Our patient's perception of the severity of the event we're trying to prevent relative to the side-effect we might cause: s
 - iv. LHH = $(1/NNT)^{*}f_{t}^{*}s$ [vs] $(1/NNH)^{*}f_{h}$

Therapy: Systematic Reviews

- 1. Is the evidence from this systematic review valid?
 - a. Is this a systemic review of randomized trials?
 - b. Does it describe a comprehensive and detailed search for relevant trials?
 - c. Were the individual studies assessed for validity?
 - d. A less frequent point:
 - i. Were individual patient data (or aggregate data) used in the analysis?
- 2. Is the valid evidence from this systematic review important?
 - a. Are the results consistent across studies?
 - b. What is the magnitude of the treatment effect?
 - c. How precise is the treatment effect?
- 3. Translating Odds Ratios and Relative Risks into Numbers Needed to Treat
 - a. When OR < 1:
 - i. NNT = 1 [PEER*(1-OR)/(1-PEER)*(PEER)*(1-OR)]
 - b. When OR > 1:
 - i. NNT = 1 + [PEER*(OR-1)/(1-PEER)*(PEER)*(OR-1)]
 - c. When RR < 1:
 - i. NNT = 1/(1-RR)*PEER
 - d. When RR >1:
 - i. NT = 1/(RR-1)*PEER
 - e. PEER = Patient expected event rate
- 4. Can we apply this valid, important evidence about therapy in caring for our patient?

- a. Is our patient so different from those in the study that its results cannot apply?
- b. Is the treatment feasible in our setting?
- c. What are our patient's potential benefits and harms from therapy?
- d. What are our patient's values and expectations for both the outcome we are trying to prevent and the adverse effects we may cause?
- e.