Considerations on Appraisal of Therapy Articles

Bias
- Example of how the study where more people die in the community than hospital.
- Correlation doesn't equal causation
- More common in observational studies, morbidity and mortality may not just be from the treatment
- Prognostic factors play a large roll in clinician recommendations, leading to bias of studies
- Often show larger effect than RCT

Randomization
- Tx and control group are much more likely to be balanced for determinants of outcome (known and unknown)
- Example of how in the 70s-80s there was extracranial intracranial bypass, nonrandomized comparisons showed benefit however w/ RCT surgery showed increased adverse outcomes soon after surgery
- Randomization is really important as sometimes we have surprising results
- Without randomization, prognostic factors can be unbalanced and you will get over or underestimation of treatment effect
  o The more prognostic factors and outcome are related the more important randomization is
- Does NOT always make groups of similar prognosis/background
  o More common if not blinded or pts aren't analyzed in the group they were allocated in
  o Small sample size
  o sometimes just bad luck

Concealment
- Example of how lap vs open appy study went well during the day being randomized, but at night the residents were looking at the envelopes to do more open, if pt was sicker -> open as well
- Without concealment – pt presentation can cause clinicians to put in tx or control group without randomization
- Ways to conceal
  o Blinded med at pharmacy
  o Remote randomization (person putting people in groups doesn't know anything about the patients)
  o Sealed envelope

Intention to treat
- AKA were pts analyzed in the group that they were randomized in
- Sometimes studies exclude noncompliant patients -> can falsely overestimate treatment
- Surgical therapies: excluding those who didn't get the surgery or those who had an outcome before the surgery (MI, CVA)
  o If put in control arm -> any surgery would look like it's helpful (even if nothing was done in the surgery)
- Intention to treat preserves the goal w/ randomization

Absolute risk

Relative risk reduction

Blinding
- Patient blindness: patient does not know what arm they are in
- Placebo effect is a real thing
- Clinician blindness: clinician does not know what arm pt is in

- o Differences in pt care based on what arm pt is in
- Outcome assessors blindness:
  - o Almost always can be blinded
- "the more judgment is involved in determining whether pt has suffered a target outcome, the more important blinding becomes"
  - o Less important in all-cause mortality bc hard to debate that

Follow up
- Lost to follow up = unknown pt status
- Validity is compromised with increasing lost to follow up bc those patients are often different than those who do follow up
  - o Different prognoses
  - o May have suffered adverse outcomes
  - o Patient doing really well and doesn't return for f/u
  - o No specific rule of thumb that determines when validity is compromised, some say 20%
- Intention to treat is important!

TABLE 1B–1

Users' Guides for an Article About Therapy

Are the results valid?

Did experimental and control groups begin the study with a similar prognosis?

- Were patients randomized?
- Was randomization concealed (blinded or masked)?
- Were patients analyzed in the groups to which they were randomized?
- Were patients in the treatment and control groups similar with respect to known prognostic factors?

Did experimental and control groups retain a similar prognosis after the study started?

- Were patients aware of group allocation?
- Were clinicians aware of group allocation?
- Were outcome assessors aware of group allocation?
- Was follow-up complete?

What are the results?

- How large was the treatment effect?
- How precise was the estimate of the treatment effect?

How can I apply the results to patient care?

- Were the study patients similar to my patient?
- Were all clinically important outcomes considered?
- Are the likely treatment benefits worth the potential harm and costs?