“A good listener helps us overhear ourselves.”

Yahia Lababidi, author (b. 1973)
Critical Appraisal

Fundamental Concepts

Objectives

• To apply basic skills of critical appraisal
• To apply fundamental principles in evaluation of research knowledge

Disclosure

No financial conflicts of interest.

Main messages

• The therapeutic encounter
• Healthy skepticism
• Common sense vs p < 0.05
• You’ve got the power
• Humility

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History

- Bloodletting
- Granville’s Hammer
- Insulin coma therapy
- Lobotomy
- Schizophrenogenic
- Valium housewife
- Serotonin theory
- Atypicals

Medical Practice

- Culture and tradition
- Confounding bias
- Measurement bias (instrument, observer, recall)
- Chance
- Conflicts of interest
- Marketing

Reversals of Established Medical Practices
Evidence to Abandon Slip

Leibovici, 2001

Retroactive Prayer…

Effects of remote, retroactive intercessory prayer on outcomes in patients with bloodstream infection: randomised controlled trial

Leibovici, 2001
Adult patients with sepsis & positive blood cultures
University hospital, 1990-1996
Randomized to 2 grps
Prayer for “well being and full recovery” for one grp

Primary outcomes
- # of deaths
- LOS
- Duration of fever > 37.5°C
Chi-squared test

Mortality
- 28.1% intervention; 30.2% ctrl
- P=0.4

Conclusions
Remote, retroactive intercessory prayer said for a group is associated with a shorter stay in hospital and shorter duration of fever in patients with a bloodstream infection and should be considered for use in clinical practice.
Hill's Criteria for Causation

- Strength (effect size)
- Consistency (reproducibility)
- Specificity
- Temporality
- Dose-Response
- Plausibility
- Coherence
- Experiment
- Analogy

Levels of Evidence

I. DBRCT, Meta-analysis/systematic review
II. Observational studies
   A. Cohort
   B. Case-control
III. Case series
     Case reports
     Expert opinion

DBRCT
Double Blind Randomized Controlled Trial

- What is the question / intervention?
- Relevant, important?
- Who stands to benefit?

DBRCT
Double Blind Randomized Controlled Trial

- What is the comparator?
- Is it appropriate?

DBRCT
Double Blind Randomized Controlled Trial

- Table 1
- Confounders accounted for?
DBRCT
Double Blind Randomized Controlled Trial

- Steps taken
- Did it work?

Methods

Subjects
- Number of sites
- Demographics
- Illness severity
- Comorbidity / substances
- Compliance
- Drug response
  - PBO lead in?
  - Intervention w/d from responders
  - Failed comparator

...Methods

- Intervention & comparator
  - Inert PBO, active PBO, active comparator
  - Dosing
- Primary outcome measures
  - Relevance
  - Clearly specified
  - One or two
- Adverse events (collection, reporting, attribution)
- Power, study length

Bias Minimization

- Randomization
  - Adequate?
  - Did it work?
- Blinding
  - Adequate?
  - Did it work?

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Results

Descriptive

Inferential

Dropouts / Deviations

• Dropout extent

• Completer / per protocol

• ITT
  – LOCF
  – Imputation

p-value...

...p-value

• Null hypothesis testing

• 1 or 2 tails

• Arbitrary

• Multiple comparisons problem

Effect Estimation...

• Percentage of responders

• Effect size

• RR, OR

• Relative risk reduction (RRR)

...Effect Estimation...

• ARR

• NNT

• NNH

• Confidence intervals
…Effect Estimation

Confidence intervals
95% CI = repeating the study, mean will be within this range 95% of time

• Statistical significance
• Range
• Effect size
• Precision

TADS (March et al, 2004)

• DBRCT, 479 adolescents
• FLX, CBT, both, PBO
• Suicidality secondary outcome
• 7 suicide attempts, 6 on FLX
• OR suicidality 1.77 (0.76-4.15)

• RR suicide attempts 6.19 (0.75-51.0)
  (Ghaemi, 2009)

SSRIs for Autism – Funnel Plot

Carrasco et al, 2012

Clinical Significance

“Enlightenment is man's release from his self-incurred immaturity. Immaturity is man's inability to make use of his understanding without direction from another. This immaturity is self-imposed when its cause lies not in lack of reason but in lack of resolution and courage to use it without direction from another. “Have courage to use your own reason!” -- that is the motto of enlightenment.”

Immanuel Kant, An Answer to the Question: What is Enlightenment?, 1784