CLINICAL RESEARCH CURRICULUM

Critical appraisal of the medical literature
Why read?

“It is astonishing with how little reading a doctor can practice medicine, but it is not astonishing how badly he may do it”
Why read?

- It is highly likely that your clinical practice will reflect your residency training for a long time; practice patterns remain constant.
- However, medical and surgical treatments and techniques are constantly changing; only constant is change.
- Physicians have a fiduciary responsibility to continually update one’s knowledge of diseases and their treatment.
- Ways of expanding your knowledge and skills:
  - Journal articles
  - Specialty meetings and CME activities
  - Colleagues in your own practice
  - Colleagues in other practices and specialties
  - Instruction Courses
Why read?

• The uncertainty of medical practice only begins after residency training
• Reading journal articles allows a surgeon to “experience” treatment and outcomes in patients not commonly encountered
• Reading journal articles allows a surgeon to compare one’s experience with that if others
  – Should be an impetus for improving one’s practice
• Continue CME to reduce uncertainty of medicine
Why read critically?

- Most surgeons “read” journal articles by scanning the abstracts
- Abstracts rarely tell the whole story, do not contain enough details or nuances, and are frequently biased
- Abstracts are the appetizers that should get your interest up, but it cannot be the main course (Methods, Results, and Conclusions)
  - The rest of the article contains the important nuances
- Beware of reading only abstracts, especially if you plan to change your practice based on the study!
Why read critically?

• “Most medical articles are biased in some way”
  • Has mostly to do with levels of evidence
  • Who writes most of the journal articles?
  • What are the associated biases?

• Bottom line:
  – Do NOT believe anything people write until you’ve convinced yourself it was a well done study with valid conclusions.
  – The data holds the truth. The review process is supposed to weed out poor studies but it is not always the case.
Critical appraisal of the Literature

- What is the objective/hypothesis of this manuscript?
  - Is it relevant for clinical care?
- What outcomes are being measured?
  - What is the data type gathered?
- Is the study biased, is there confounding, can the results be explained by chance?
  - Subject selection, data collection proper?
- Are the conclusions supported by the study data?
  - Appropriate statistics, adequate power?
- Was the study ethical and without conflict of interest?
- Are the findings clinically relevant?
Types of Medical Articles

• Original Scientific Research
• Reviews (Scientific, meta-analysis)
• Short (Rapid) Communications
• Case Reports
• Clinical photographs
• Letters to the Editor
• “How I Do It”
Step 1: Assess if the article is relevant?

- Can the information in this study be used to improve patient care and public health?
Step 2: What type of study is it?

• Descriptive studies
  – Data used for descriptive purposes and not used to make predictions
  – Correlational studies, case reports or series, cross sectional surveys
  – Measures of central tendency (mean, median, mode)

• Inferential studies
  – Use data from study sample to derive conclusions and/or make predictions about the population
  – Statistics used to prove or reject hypothesis
Step 2: What type of study is it?

• Therapeutic studies
  – Investigate the results of treatment.

• Prognostic studies
  – Investigate the effect of a patient characteristic on the outcome of the disease

• Diagnostic studies
  – Investigate a diagnostic test

• Economic and decision analysis
  – Develop an economic or decision model
Step 3: What is the intervention?

- What are the dependent, independent, and confounding variables of the study?
Step 4: Who are the subjects

- Who are the subjects?
  - The ideal patients to study is from a random sample
  - In fact, most studies do not use a totally random sample, thus introducing selection bias
  - Review subject inclusion/exclusion criteria carefully to determine if the subjects are similar to your patients and to assess external validity
Step 5: Is the study internally valid? aka Do I believe the study?

- Internal validity
  - Credibility of the findings for the study sample
  - Look at objectives then conclusions
  - Then need to assess if the conclusions are supported by the study by confirming:
    - Proper study design (Methods)
    - Unbiased measurements of outcome measures (Methods)
    - Appropriate statistical analysis of data (Results)
Internal validity
Assess hypothesis/objective of the study

Hypothesis/Objectives

• Research hypothesis → what the researcher predicts
• Null hypothesis (Ho) → there is no difference in outcome between the two groups; in general expect the null hypothesis to be rejected because researcher usually predicts a difference between groups
• Alternate hypothesis (H1) → there is a difference between the groups; typically, researcher expects this to be supported so this is the research hypothesis
What type of study is it?

- Levels of evidence
  - 1. Level 1: Randomized controlled trial
  - 2. Level 2-a: Controlled trial without randomization
  - 3. Level 2-b: Cohort or case-control studies
  - 4. Level 2-c: Uncontrolled trials, nonrandomized cohort
  - 5. Level 3: Case series, case reports, expert opinion, conclusions extrapolated indirectly from scientific studies
• **Randomized trial**
  – Interventions are randomly allocated
  – Both treatment and control groups are equally eligible subjects
  – Best design is when neither the investigator nor the subject know which group they are in (double blinding)
  – Usually the best research approach
  – However, bias is likely to occur if the hypothesis has not been generated *a priori*
• **Cohort study**
  - A cohort is a group of subjects followed forward in time
  - Best for defining the incidence of and potential causes of a condition
  - Expensive and inefficient way to study rare outcomes
  - Prospective cohort studies become more efficient as the outcomes become more common
Case-control studies

- Select a group of subjects with a condition (cases), then look for risk factors, and compare with a group of similar subjects without the condition (controls), then look for similar risk factors
- Much cheaper to do this type of study than cohort or cross sectional studies
- Potential biases include sampling bias and differential measurement bias (because data collection begins after the event of interest)
• **Case series and reports** (most articles in otolaryngology journals are of this type)
  – Has a high probability for bias
  – These studies must present
    • A priori protocol to collect and analyze data
    • Include all eligible subjects in a specified time period
    • Have follow-up data for at least 80% of enrolled subjects
    • Follow-up duration must be adequate
    • Present complete outcomes
Internal validity

Reject or support the hypothesis?

• Need proper Statistics 😞
• Research involves measurement of data
• Evaluation of the data for significance (hypothesis testing) requires knowledge of statistical principles
• The data type that is collected decides the type of statistics that should be used for hypothesis testing
Assess data measurement

• How was the data measured?
  – Who measured it?

  • Typically want the individual collecting and interpreting the data to have no knowledge of the treatment rendered
  • Always assume bias if that is not the case
  • Then have to decide how much bias there may be in collection, analysis, and interpretation of data
  • If the unblinded treating individual is also collecting and interpreting the data there is potential for bias.
Assess adequate sample size

• Especially important for descriptive statistics
  – 83% success rate in 6 patients is different from same success rate in 600 patients

• In general, inferential statistics take sample size into consideration
  – Results may trend towards significance ($p = 0.05$) with low sample size but become significant if more subjects were enrolled

• In research design, however, power calculations should be done to assess adequate sample size
Look for Sources of Bias in the Study

• Bias
  – Things that may influence the research and lead to a systematic deviation from the truth
  – May occur in each stage of data manipulation:
    • Collection
    • Analysis
    • Interpretation
    • Publication
    • Review
Few examples of Bias

- Design bias
- Ascertainment bias
- Selection bias
- Observer bias
- Reviewer bias

- See next week’s article to get the list of different types of bias
Look for Confounding Variables

• A confounding variable is one that is associated with the predictor variable and is a cause of the outcome variable
  – Example: An association was seen in a study between coffee drinking and MI.
  However, if more coffee drinkers were also smokers then smoking is the confounding variable
- So need to know other risk factors for disease
- Randomization reduces confounding but this research design is not always possible
Look for adequate follow-up

• In general the follow-up should be at least 80%.
• Inadequate follow-up or too many loss to follow-up is a serious flaw in research;
  – What if only the happy patients followed up with the study?
• The authors should account for all patients lost to follow-up, and at least discuss the potential bias and data scenarios
Assess statistical measures used and findings

• What is the data type measured for outcomes?
  – Nominal (categorical)
  – Ordinal (rank order)
  – Continuous
  – Ratio
• Check that proper statistical analysis was performed; example,
  – Categorical data \(\rightarrow\) chi square
  – Ordinal data \(\rightarrow\) Mann - Whitney U Test, spearman’s rho, weighted kappa
  – Continuous data \(\rightarrow\) t-test, Z-test
• Keep a statistical reference book handy to review new statistical terms while reading journal articles until familiar with it
• When a difference is shown, it could be due to (1) chance or (2) a true finding:
  – Chance (Type I error), False positive
  – Generally we accept less than 5% chance of type I error; so check that alpha level (P value) is set at \( \leq 0.05 \) for level of significance.
• When no difference is found (accept null hypothesis), it could be the truth or it could be false negative (Type II error, beta)
  – Beta is typically set at 20%
  – Power of the study is defined as the probability of true positive (accept alternate hypothesis), typically 0.80 (i.e. there is an 80% chance of detecting the difference if one truly exists)
Step 6: Is there external validity?

• External validity
  – Generalizability of the study to other population across
  – Can you safely generalize the internally valid findings to the general population
  – Was the study sample chosen appropriately and described in adequate detail for results to be generalized
  – Requires good sampling scheme, subject selection criteria, descriptive characteristics of the study sample
Step 7: Was the study ethical?

• Was the study original, approved by an IRB, and free of conflicts of interest?
Do authors report financial relationships that can bias findings?

• Most important to report financial relationship in industry supported research
• Industry supported research is 3-4 times more likely to reach pro-industry conclusions
• Editors, reviewers, and readers must all assess if a competing interest causes bias
Is there Disclosure?

• Disclosure
  – “the act of revealing something”

• Medical Disclosure
  – Author, editor, and reviewer must disclose any financial or personal relationships that inappropriately influence (bias) his or her actions
Step 8: Final thoughts
Did I get something out of this?

• Does the article significantly improve the knowledge base beyond what is already published on this topic?
• Is the statistically significant difference clinically significant?
  – Use research findings to meet the clinical needs of the patients
  – In clinical practice patient factors determine the treatment course; however, be well informed