How to Evaluate Primary Literature

Busy Day Tool Kit Preceptor Instructions

Learner level: IPPE and APPE Students

Estimated time to complete: May take several hours/days and can be done intermittently while completing other assigned projects.

Preceptor Instructions: Select a journal article relevant to current practice and/or ask the student to select a journal article that they think might help them enhance their understanding of the current rotation. Request that the student provide written completion of the module by answering the questions provided. Set up a time with your student to review the results of the completed module.

Student Instructions: Read through the module. Read the journal article. Complete the questions provided in the module and write up the review. Set up a time with your preceptor to review the results of the completed module. Provide feedback to your preceptor on the usefulness of the points analyzed.

How to Evaluate Primary Literature

Components of a Primary Literature Article

1. Authors, Journal, Year
    a. Authors
        i. ***When evaluating the authors, think about:***
            1. Do the authors/investigators appear qualified to conduct the study?
            2. Are they affiliated with major universities or industry?
            3. Was the study conducted in a reputable medical center or university teaching hospital?
            4. Have the authors published extensively on this topic?
    b. Journal- Should be an appropriate choice for the literature being published
        i. ***When evaluating the journal, think about:***
            1. Is the journal peer-reviewed or pay?
            2. Is the journal reputable?
            3. Is the journal a throwaway journal?
    c. Year
        i. When evaluating the year, think about:

1. Has the gold standard therapy changed since the article was published?
2. Was an appropriate comparator used based on availability when the study was conducted?
3. Does more recent data exist?

2. Title & abstract
    a. Reflective
    b. Should convey the purpose of the study
        i. ***When evaluating the title, think about:***
            1. Is the title consistent with the scope of the study?
            2. Is the title easy to read and clear?
            3. Does the title fairly represent the entire study?
    c. An abstract in this context is considered to be a concise overview of the study or a synopsis of the major principles of the article ("road map"). Should include the article objective, methods, results, and conclusions.
            1. Primary use of abstracts
            2. Consistency
        ii. ***When evaluating the abstract, think about:***
            1. Does the abstract fairly represent what is presented in the entire study?
            2. Does the abstract serve as a road map for the study or does it only overview a portion of the paper?

3. Introduction - serves 2 purposes: discuss the study rationale and study purpose.
    a. Study objective
    b. ***When evaluating the introduction, think about:***
        i. Is there a clear statement of purpose telling the reader why the study was done?
        ii. Are applicable and appropriate references cited that support the purpose?
        iii. Is the study appropriate and relevant?

4. Methods = study plan, most important component of a study
    a. Important for the results of the study to be valid. Flaws within the design limit the application and significance of the results.
    b. Should achieve the study purpose and test the stated hypothesis
    c. Preliminary questions to ask:
        i. Why was the study done and what clinical questions were the authors addressing?
        ii. What type of study was done?
        iii. Was the design appropriate to the research hypothesis?
    d. ***When evaluating the hypothesis, think about:***
        i. What question was the study trying to answer?

5. Methods – study design
    a. Study question dictates which study design is selected to conduct the research
    b. ***When evaluating study design, think about:***
        i. What was the nature of the design (cross-over, comparative group) and was it appropriate considering the disease and drugs under investigation?

6. Methods – sample selection
    a. Inclusion/exclusion criteria
        i. Should reflect the typical patient population who will receive the therapy in real practice
        ii. Proper inclusion and exclusion criteria allows for the study to be applied in practice.
        iii. Be aware of a possible selection bias can occur due to various reasons, but can seriously affect the study results in a negative fashion.
    b. Subject recruitment
        i. 4 main strategies
        ii. Methods in which subjects are recruited may affect generalizability
    c. ***When evaluating sample selection, think about:***
        i. Is the sample size large enough?
        ii. Are the inclusion and exclusion criteria clearly defined?
        iii. Is the sample representative of the general population?
        iv. How were the subjects recruited?

7. Methods – Controls
    a. Intervention vs Control group
    b. Different types of controls: historical, placebo, or active
        i. Historical controls
            1. Advantages/Disadvantages
        ii. Placebo controls
        iii. Active controls
    c. ***When evaluating control groups, think about:***
        i. Is the treatment control historical, placebo, or an active agent?
        ii. Is the control group used appropriately to accomplish the study objective?

8. Methods – Blinding
    a. Technique in which subjects and/or investigators are unaware of who is in the intervention or control group.
    b. Used to reduce potential bias.
    c. 3 types
        i. Single and no blinding
        ii. Double-blinding
        iii. Triple blinding
    d. ***When evaluating blinding, think about:***
        i. Is a blinding technique used to reduce the effect of bias?
        ii. What type of blinding is used in the study?
        iii. Is the blinding technique effective to accomplish the study objective?
        iv. Was the blind broken?

9. Methods - Randomization
    a. Definition
    b. Minimizes bias
    c. Many different techniques available.
    d. ***When evaluating randomization, think about:***
        i. Was the sample selected randomly or without bias?

10. Methods - Outcome measures/Endpoints
    a. All trials specify one effect caused by the intervention and control as the primary endpoint, which can be referred to as "what did the investigators measure to achieve the study objective?" Researchers may also measure secondary endpoints.
        i. Should be defined prior to the study
        ii. Should be reliable (consistent upon testing multiple times)
        iii. Should be reproducible (similar if performed under different conditions)
        iv. Should be valid (measure what they are supposed to measure)
    b. Investigators may combine a group of endpoint measures into one primary endpoint referred to as a composite endpoint.
        i. Rationale
        ii. Should be reported and analyzed separately
            1. Beware
            2. Advantages/Disadvantages
    c. ***When evaluating outcome measures, think about:***
        i. What were the primary and secondary outcome measures?
        ii. Were the outcome measures objective or subjective?
        iii. Were the endpoints clinically relevant?
        iv. Were there clear definitions of what was measured?
        v. Was the outcome measure appropriate to the goals of the study?
        vi. Were the disease parameters relevant to the objectives of the study?
        vii. Were the measurements and observations reliable and reproducible?
        viii. If tests for surrogate outcome measures were used, were the test results strongly associated with clinical outcomes?
        ix. Were side effects accounted for in the outcomes?
        x. Could observer bias have influenced the measurements or observations?
        xi. Were any important outcome measures omitted?
        xii. Were tests used sensitive and specific?
        xiii. Were the methods and research tools used appropriately?
        xiv. Was the research tools used validated or accepted?

11. Methods - Study duration
    a. Depends on the type of trial.
        i. Things to think about
    b. ***When evaluating drug administration, think about:***
        i. Were doses of the agent(s) appropriate?
        ii. Were dosage forms and route of administration appropriate?
        iii. Were administration times appropriate?
        iv. Was the duration of therapy adequate?
        v. Was compliance with therapy adequate?
        vi. Was blinding maintained?

12. Methods – Follow-Up/Data Collection/Compliance/Monitoring
    a. Should occur at predetermined intervals throughout the duration of the trial
    b. Compliance

13. Methods – Statistics
    a. ***When evaluating statistics, think about:***
        i. Are the statistical methods described?
        ii. Are the statistical tests appropriate for the data and study design?

iii. Are p-values significant?
iv. Are statistically significant differences clinically significant?

14. Results
    a. Look at data regarding follow-up and compliance.
        i. Summary of Study Groups
            1. Determine if the study groups were similar
            2. Outcomes of all participants should be known including withdrawals, deaths, and protocol violations
        ii. Reasons for not completing the trial
            1. Dropouts
        iii. Compliance measurement
    b. Intention-to-treat versus per protocol analysis
    c. Data from the primary and secondary objectives, often referred to as endpoints, should be presented clearly and completely, using clear and unbiased methods.
        i. Measurable Parameters Identified
            1. All measurements summarized and reported
            2. Data fully and clearly displayed for reader interpretation
            3. Statistical analysis provided
        ii. Evaluating Tables
            1. Are the authors counting patients or number of observations in the tables?
            2. Do the numbers in the tables add up?
            3. If percentages are used, are they calculated correctly?
            4. Can you tell what the percent was taken from (i.e., denominator)?
        iii. Use of Graphs
            1. Creates the potential for greater detail (and complexity) than tables
            2. Useful to show multiple observations on individual groups
            3. Are the figures correctly titled and labeled?
            4. Are the intervals appropriate?
            5. Are the scales appropriate?
            6. Have data been omitted?
                a. Are summary data presented?
                b. Are the graph characteristics correct?
    d. Outcome measures may be also be <u>surrogate endpoints</u>
            1. Definition
            2. Examples
    e. Subgroup analysis
        i. Limitations
    f. Ancillary therapy
        i. Should they be allowed?
    g. Adverse Event Data
    h. ***When evaluating the results, think about:***
        i. Do the results make sense?
        ii. Has any data been omitted?
        iii. Were all patients accounted for?
        iv. Was this an intent-to-treat analysis?
        v. Could a Type I or Type II error explain the result?
        vi. Were p-values and/or confidence intervals provided?
        vii. Are all primary and secondary outcome measure results provided?

15. Discussion
    a. Summary of the key finding of the study including explanations of study results.
    b. Discuss how study affects practice.
    c. Strengths & limitations should be discussed.
    d. ***When evaluating the discussion, think about:***
        i. Is biased language used throughout the discussion?
        ii. Have related publications been appropriately referenced or is there a biased subset that has been presented for comparison?
        iii. Are the results statistically significant and are they clinically significant?
        iv. Have inappropriate conclusions been drawn that are not supported by the data?
        v. Have inconsistencies, study limitations, and dropouts been addressed?

16. Conclusion & References
    a. ***When evaluating the conclusion, think about:***
        i. Are the conclusions of the author supported by the data?
        ii. Are conclusions relevant to the objective or purpose of the study?
        iii. Do you accept or reject the author's conclusion?
    b. ***When evaluating references, think about:***
        i. Number of references
        ii. Publication year of the references
        iii. Percentage of references from the primary literature
        iv. Authors citing their own work

References

Chapman JT. (personal communication, July 2005).

Kendrach M, Freeman MK, Wensel TM, Hughes PJ. Literature Evaluation I: Controlled Clinical Trial Evaluation. In: Malone PM, Kier KL, Stanovich JE. *Drug Information: A Guide for Pharmacists.* 4th ed. New York, NY: McGraw-Hill; 2012: 111-172.