Module 6. Practicing Evidence-Based Medicine

EDUCATIONAL OBJECTIVES

Upon completion of this activity, participants will be better able to:

1. Interpret common elements of clinical trial design;
2. Discuss the strengths and limitations of a clinical trial;
3. Demonstrate how to find clinical practice guidelines; and
4. Apply primary literature and other high quality drug information to the clinical decision-making process.

Post-Test/Rationale

1. From which of the following study designs can conclusions regarding causality be made?

   A. case-control
   B. cross-sectional
   C. retrospective cohort
   D. prospective interventional

Correct Answer: D
Conclusions regarding causality can only be made from interventional studies. Case-control, cross-sectional, and retrospective cohort studies all have observational designs. Observational studies cannot lead to definitive conclusions regarding causality of drug-related effects since these study designs are more likely to have confounding factors than interventional studies.

2. The potential is reduced for BOTH bias and confounding with which of the following clinical trial element(s)?

   A. blinding
   B. randomization
   C. use of a control group
   D. all of the above

Correct Answer: B
Randomization reduces the potential for bias in treatment allocation. Randomization can also minimize confounding by ensuring that important characteristics are balanced among treatment groups, especially when stratified randomization is used. Blinding only minimizes bias, not confounding. Use of a control group allows for treatment comparisons but does not affect either bias or confounding.

3. Choose the CORRECT statement:

   A. The potential for Type I error is limited to 20% in clinical trials with 80% power.
   B. Noninferiority trials seek to establish that one treatment is at least as good as another.
C. Intention to treat analyses are preferred because they maintain randomization and mimic real life practice.***

D. Mean and standard deviation are the appropriate measures of central tendency and variability, respectively, for ordinal data.

**Correct Answer: C**

In general, intention to treat analyses are preferred because they maintain the original randomization scheme and mimic the imperfect patient compliance/follow-up that occur in actual clinical practice. The other answer choices are incorrect statements. The potential for Type II error (not Type I error) is limited to 20% in clinical trials with 80% power. Noninferiority analyses seek to establish that one treatment is not inferior to another treatment. The measures of central tendency and variability for ordinal data are median and confidence interval, respectively.

4. Which of the following clinical trials has the HIGHEST internal validity?

   A. An open-label, randomized, equivalence trial comparing 2 antibiotic regimens for treatment of community-acquired pneumonia in China
   B. A randomized, double-blind trial with very strict inclusion and exclusion criteria that used subtherapeutic doses of the active control medication
   C. A double-dummy trial that used stratified and block randomization to assign patients to either an oral active therapy, parenteral active therapy, or placebo, with all other aspects of the study protocol according to the institution’s “usual care”***
   D. A randomized, double-blind, Phase III clinical trial conducted in the United States and Europe that compared a new medication with placebo for treatment of moderately-severe Type 2 diabetes

**Correct Answer: C**

Clinical trials with a low potential for bias and confounding have high internal validity. Double-dummy blinding minimizes bias, especially when different routes of administration are used. Randomization that includes both stratification and blocks minimizes the potential for confounders.

5. Which of the following clinical trials has the HIGHEST external validity (assume U.S. clinical practice)?

   A. An open-label, randomized, equivalence trial comparing 2 antibiotic regimens for treatment of community-acquired pneumonia in China
   B. A randomized, double blind trial with very strict inclusion and exclusion criteria that used subtherapeutic doses of the active control medication
   C. A double-dummy trial that used stratified and block randomization to assign patients to either an oral active therapy, parenteral active therapy, or placebo, with all other aspects of the methods according to the study institution’s “usual protocols”
D. A randomized, double blind, Phase III clinical trial conducted in the U.S. and Europe that compared a new medication with placebo for treatment of moderately-severe Type 2 diabetes***

Correct Answer: D

External validity is an assessment of how readily study results can be extrapolated beyond the study population. Geography and ethnicity are a component of Type 2 diabetes prevalence, response, and progression, so a study conducted in the U.S. would have the highest external validity. The inclusion and exclusion criteria should also be considered. Studies with stringent inclusion and exclusion criteria may be difficult to extrapolate beyond the study population.

6. Choose the CORRECT clinical trial outcome/outcome description pairing below.

A. patient-reported compliance/single safety outcome  
B. heart failure exacerbation rate/single surrogate outcome  
C. change in blood pressure from baseline/single surrogate outcome***  
D. rate of myocardial infarction, stroke, hospitalization, or all-cause mortality/composite of surrogate outcomes

Correct Answer: C

Change in blood pressure from baseline is a single outcome (not a composite outcome). Change in blood pressure is a surrogate measure of risk for major cardiovascular outcomes such as myocardial infarction, stroke, or cardiovascular death.

7. What is the equation to calculate number needed to treat (NNT)?

A. 1/ARR***  
B. 1/RRR  
C. 1-ARR  
D. 1-RRR

Correct Answer: A

The number needed to treat (NNT) is calculated as 1/ARR.

8. Which of the following searches would be MOST likely to yield a rheumatoid arthritis clinical practice guideline?

A. Search PubMed and limit to “Review Articles”  
B. Google search “how do I treat rheumatoid arthritis?”  
C. Search the American College of Cardiology website  
D. Search the National Guideline Clearinghouse website***

Correct Answer: D

Of these answer choices, only the National Guideline Clearinghouse website would be likely to yield a clinical practice guideline for rheumatoid arthritis. Clinical practice guidelines can also be found by searching the authoring organization’s website or the primary literature.
9. Choose the CORRECT statement regarding the evidence-based medicine process.

A. The clinical question should be defined as generally as possible
B. Quality of all information sources can be considered equivalent
C. The first information retrieved should be used for the recommendation
D. The final recommendation should incorporate quality evidence, clinical judgment, and patient preferences***

Correct Answer: D
Evidence-based medicine is the process of applying high quality information to answer specific questions about patient care decisions. All available information should be considered after completing a systematic and thorough search. The final clinical recommendation should include the patient’s current clinical situation, patient preferences and actions, and the provider’s clinical expertise in addition to the evidence.

10. A clinical pharmacist has been asked by a physician to recommend a new medication for neuropathic pain that is least likely to interact with a patient’s multiple other medications. After searching clinical practice guidelines, primary literature, and drug interaction resources, the pharmacist has narrowed the options to pregabalin (Lyrica) and topiramate (Topamax). Which of the following factors would likely be MOST relevant for the pharmacist to consider when making an evidence-based recommendation?

A. primary literature quality, symptom severity, insurance coverage***
B. dosing frequency, boxed warnings, patient preference for capsules or tablets
C. approval status for neuropathic pain, patient hepatic function, availability of a liquid dosage form
D. working relationship between the physician and pharmacist, recent quality improvement strategies within the organization, pharmacist’s anecdotal experiences with patients on both medications

Correct Answer: A
Evidence-based clinical recommendations should include the patient’s current clinical situation, patient preferences and actions, and the provider’s clinical expertise in addition to the evidence. Of these answer choices, only the correct answer considers published literature in addition to patient- and provider-specific factors.