MODULE 1: 
Clinical Study Designs: 
Basics and Biases

Watch this video overview of module 1.

Clinical studies are done for a variety of reasons. They are commonly conducted to determine if a treatment is effective or more effective than another treatment, to determine prognosis of disease, to study how good a diagnostic test is, and to study potential risk factors and their associations with disease. Our own unsystematic observations in the clinic or in the hospital can be misleading because we only see a small, biased sample of people with a given problem. Studies can enroll larger numbers of people and can be systematically conducted thus yielding “better” answers.

In this module you will learn about various study designs. You will learn about why certain studies are chosen to answer certain types of questions. You will also learn about the common biases (systematic errors that cause the findings to deviate from the truth) that can affect each study design. (🎧 EBM secret: critical appraisal checklists are used to detect these biases.)

Teaching point: It's important that residents understand that someone needs to critically appraise an article they potentially want to use to answer a clinical question. They should first look to the pre appraised literature for an answer. (Hopefully you are teaching them about the Alper and Haynes EBM Pyramid 5.0.) If it's not available there and they have to use a primary article then they must do the critical appraisal themselves. Most medical students and residents use UpToDate or Dynamed. They need to understand there is a delay in studies getting entered into these tools and that not every study makes it into these tools. Thus, they need to understand critical appraisal is a necessary tool for lifelong learning. They should know that various critical appraisal checklists are freely available on the internet and they should use them every time they read a primary study.
Observational Studies

Try to answer these questions as you work through this section of the module:

- Compare and contrast cohort and case-control studies. How are they different? What are the advantages of cohort studies? What are the advantages of case-control studies?
- What is the key element in selecting controls in case-control studies?
- Why are retrospective studies more prone to bias than prospective studies?

- **Lecture notes**: read these [lecture notes](#) to get an overview of observational studies.

- **Videos**: watch these videos for an overview of each study design.
  - [Overview of study designs](#) (watch first 1:43 only)
  - [Cohort Studies: A Brief Overview](#), (5:33)
  - [Case Control Studies: A Brief Overview](#), (4:57)

- **Readings**: read these for an overview of each study design.
  - Users' Guides to the Medical Literature: A Manual for Evidence-Based Clinical Practice, 3rd ed [Chapter 14: Harm (Observational Studies)](#)
  - Fletcher Chapter 5 pages 61-left half of 67 (beginning of chapter to ways to express and compare risk)
  - Fletcher Chapter 6 pages 80-87 (beginning of chapter to the odds ratio)
  - [Case-control studies: research in reverse](#)
  - [Cohort studies: marching toward outcomes](#)
Randomized Controlled Trials

Try to answer these questions as you work through this section of the module:

- How do RCTs differ from observational studies? How are they the same?
- What is the difference between efficacy and effectiveness?
- Why is randomization important?
- Why is blinding important? What are the different types of blinding?
- What are the 2 approaches to analyzing RCTs? What are the pros/cons of each?

- **Lecture notes:** read these lecture notes to get an overview of RCTs.
- **Videos:** watch these videos for important aspects about RCTs.
  - Why Randomization Is Important (5:02)
  - Blinding in Clinical Trials (7:14)
  - Intention-to-treat analysis (4:43)

- **Readings:** read these to understand important aspects about RCTs.
  - Users' Guides to the Medical Literature: A Manual for Evidence-Based Clinical Practice, 3rd ed Chapter 7: Therapy (Randomized Trials)
  - Fletcher Chapter 9
  - Fletcher Chapter 1 pages 8-10 (section on confounding)
  - Understanding controlled trials: Why are randomised controlled trials important?
  - Allocation concealment in randomized trials
  - The Intention-to-Treat principle how to assess the true effect of choosing a medical treatment
Diagnosis and Screening

Try to answer these questions as you work through this module:

- How do I choose a diagnostic test? When should a sensitive test be used? When should a specific test be used?
- How is screening different than diagnosis?
- Why is survival a bad outcome to use in a screening study?

- **Lecture notes:** read these lecture notes to understand more about diagnostic and screening test studies.
- **Videos:** watch these videos for important aspects about diagnostic and screening studies.
  - [How to Choose a Diagnostic Test](#) (7:16)
  - [Screening vs diagnostic tests](#) (7:03)
- **Readings:** read these to understand more about diagnostic tests and screening.
  - Users' Guides to the Medical Literature: A Manual for Evidence-Based Clinical Practice, 3rd ed Chapter 18: Diagnostic Tests
  - Fletcher Chapter 8
  - Fletcher Chapter 10 (stop at incidentalomas)

Biases

Bias is a systematic error that causes the results of a study to deviate from the truth. Each study design has its own unique set of biases that it can fall victim to. Critical appraisal checklists are designed to detect these biases.

**Teaching point:** The Users’ Guides are just a collection of very basic questions to detect the most important biases in studies. The Users’ Guides will be fine for most students. For those doing research (especially systematic reviews) more advanced checklists are used. This is because the answers to the Users’ Guides questions are in a yes or no format. Sometimes things are partially done in a study or done but not done well and the Users’ Guides can't really account for this degree of detail. Most study designs have more advanced, validated bias checklists that have been published. Discussion of these is beyond the scope of this course. Should
you want more information on a more advanced checklist please feel free to contact me at terry@uab.edu

Try to answer these questions as you work through this module:

- How is bias different from random error?
- What 4 things can explain every study finding?
- What are some ways these biases can be minimized in designing studies?

- **Lecture notes:** read these [lecture notes](#) to understand the common biases that can affect various study designs.

- **Videos about biases:**
  - [Bias & Validity Definition in Research Study Design](#) (6:38) - general overview of bias
  - [USMLE Step 1 Epidemiology Principles: Bias](#) (watch up to 12:43)
  - [Selection, measurement, and misclassification bias](#) (17:01)
  - [How to Critically Appraise a Diagnostic Test Study](#) (13:26) - just skip around to the discussions of the various biases
  - [What Is Lead Time Bias?](#) (2:46)
  - [What Is Length Time Bias?](#) (2:46)
  - [Overdiagnosis bias](#) (13:50)

- **Readings about bias:**
  - Users' Guides to the Medical Literature: A Manual for Evidence-Based Clinical Practice, 3rd ed [Chapter 6: Why Study Results Mislead: Bias and Random Error](#) (general overview)
  - Understanding sources of bias in diagnostic accuracy studies
  - [Online catalogue of biases](#)
  - Fletcher Chapter 1 (pgs 7-8, bias section stopping at confounding)
  - Fletcher Chapter 8 (pgs 116-117 spectrum of patients and bias, stop at chance)
- Fletcher Chapter 10 [pgs 160-162 (lead time bias, length time bias, compliance bias) 167-169 (overdiagnosis and incidentalomas)]

**Videos about critical appraisal:**
- How to Critically Appraise a Diagnostic Test Study (13:26)
- How to Critically Appraise a Harm Study: Part 1 (5:41)
- How to Critically Appraise a Harm Study: Part 2 (7:11)
- How to Critically Appraise a Prognosis Study (14:46)
- How to Critically Appraise a Therapy Study-Part 1 (9:08)
- How to Critically Appraise a Therapy Study-Part 2 (9:38)
- How to Critically Appraise a Systematic Review: Part 1 (7:41)
- How to Critically Appraise a Systematic Review: Part 2 (4:56)

**Readings about critical appraisal:**
- Users' Guides to the Medical Literature: A Manual for Evidence-Based Clinical Practice, 3rd ed. Chapter 18: Diagnostic Tests (read the “Are the Results Valid?” section)
- Users' Guides to the Medical Literature: A Manual for Evidence-Based Clinical Practice, 3rd ed. Chapter 14: Harm (read the “Are the Results Valid?” section)
- Users' Guides to the Medical Literature: A Manual for Evidence-Based Clinical Practice, 3rd ed. Chapter 20: Prognosis (read the “Are the Results Valid?” section)
- Users' Guides to the Medical Literature: A Manual for Evidence-Based Clinical Practice, 3rd ed. Chapter 7: Therapy (read the “Are the Results Valid?” section)
- Users' Guides to the Medical Literature: A Manual for Evidence-Based Clinical Practice, 3rd ed. Chapter 22: The Process of Systematic Review and Metaanalysis (read the “Are the Results Valid?” section)
After critically appraising a study readers have now determined if one of four explanations for a study result is present (ie bias). In module 2 you will learn about another one...chance and in module 5 you’ll learn how to detect confounding.