What Is “Evidence-Based Clinical Practice”?
Outline of Module

- This module will introduce the following topics:
  - A Very Brief History of Evidence-based Clinical Practice (EBCP)
  - Rationale for EBCP
  - Essential Steps of EBCP
  - Framework for learning EBCP
  - Introduction to Common Research Study Designs in Medicine
  - “Interventional” vs. “Observational”
  - Levels of Evidence
Objectives of Module

- Students who complete this module should be able to:
  - Provide a rationale for learning evidence-based clinical practice.
  - Describe the essential steps of EBCP
  - List the most common basic study designs used in medicine
  - Identify the key difference between experimental and observational study designs
  - Explain why all research evidence is not of equal importance in the practice of medicine
Evidence in Clinical Practice
Evidence in Medicine – A Brief History

Since at least the time of Hippocrates, physicians have attempted to promote health and healing using the best knowledge available. However, what qualifies as “evidence” for medical knowledge and how “evidence” can be determined have changed greatly over history.

The term “evidence-based clinical practice” (or EBCP) refers specifically to the incorporation of scientific studies into patient care and the appropriate evaluation and analysis of evidence in clinical decision-making.

While the use of various types of evidence in medicine is long-standing, the discipline of EBCP is relatively new.

Drs. David Sackett and Gordon Guyatt of McMaster University (Canada) are generally considered the “fathers” of evidence based medicine (EBM)

The term “evidence-based medicine” was first used in a series of articles in JAMA in the early 1990s, which form the basis for the current text, “User’s Guide to the Medical Literature”

More recently, the phrase “evidence-based clinical practice” has come into use. The new phrase emphasizes the practical aspects of the discipline, as well as its use by non-physician team-members (e.g., nurses, social workers).*

*Note: In the literature, as well as here, the terms EBM and EBCP are used interchangeably.
What Counts as “Evidence”? 

- There are many sources of information that a clinician might use to treat a patient:
  - Studies quantifying risks and benefits of treatments for patients with certain characteristics (e.g., age, sex, race, behavioral habits)
  - Molecular or physiological studies regarding the effects of certain treatments
  - Previous experiences having treated this patient or other patients
  - Information about costs of and access to treatments (e.g., does the hospital formulary contain the drug? will insurance pay for it?)
  - Ethical and legal knowledge of the patient’s rights and a physician’s duties
  - Understanding gained from talking with the patient about their particular goals and values in this particular situation
The “Evidence” in EBCP

- Evidence-based clinical practice involves the skills of acquiring, analyzing, and synthesizing these various types of information. It also involves applying this information for the benefit of the patient.

- The development of these skills is a primary goal of your education as a clinician. You will develop them through training and practice, very similar to learning communication skills and physical exam skills.

- Specifically, practicing EBCP means integrating information from clinical experience with the goals and values of individual patients and the best available evidence from scientific research.

- The goal of these modules is to provide a foundation for the integration of clinical research into your medical training and practice.
The Need for EBCP
The Need for EBCP

- EBCP is, in part, a response to the growing quantity of medical knowledge, treatments, and technologies available to clinicians.
  - The amount of medical knowledge available today is enormous and growing

Imagine, for example, the predicament of a patient presenting to a physician’s office with diabetes type II, a deficiency in insulin and excess of glucose in the blood.

- There are a number of treatments available to help this patient. These include:
  - Medications: at least 7 classes of medications now available, which work in different ways to lower blood sugar levels: sulfonylureas, biguanides, meglitinides, thiazolidinediones, DPP-4 inhibitors, SGLT2 inhibitors, and alpha-glucosidase inhibitors
  - Insulin therapy: short-acting injections, long-acting injections, pump
  - Behavioral interventions: diet, exercise
  - Surgical interventions

- The molecular and physiological aspects of these treatments have been well-characterized. The treatments have been shown to work in people.
  - However, not all of these treatments are equally beneficial for all patients.

How can a clinician choose the best way to help this patient?
Some Ways Decisions Are Made...

- **Decision-making by anecdote** ("Last time I gave metformin, it worked just fine.")
  - Story-telling has an important place in medical practice
    - It provides a way for us to understand our patients and may help us remember medical knowledge
  - However, it has obvious limitations especially for new clinicians!

- **Decision-making by expert opinion** ("My mentor always said to give glipizide.")
  - Expert opinion also has a role in your training
    - In the hospital, trainees learn directly from those with more experience
  - However, this method also presents limitations
    - Imagine a situation when experts disagree—then how do you decide which one is right?

- **Decision-making by convenience** ("What medications do we have in the sample closet right now?")
  - Almost never an appropriate way to make medical decisions – but you may well see it happen...
More Ways to Make Decisions

- **Decision-making by headline or sound byte or glossy advertising** ("The pharmaceutical rep showed me a graph that made pioglitazone look pretty good.")
  - It is not a good idea to make decisions based on an incomplete understanding of something you’ve read or heard
    - If a patient were to say to you “Well, I read it on the Internet,” or “I heard it on the news,” you would still want to know all of the details
  - EBCP requires thorough and thoughtful interpretation of clinical research

- **Decision-making by pathophysiological reasoning** ("It seems reasonable that the patient would only need insulin after meals, as that is when blood sugars will be highest")
  - Much medical knowledge relies heavily on pathophysiological reasoning
    - Such reasoning often forms the basis for drug discovery, disease characterization, and aspects of clinical problem solving
  - However, this reasoning may often be incorrect when used alone
    - EBCP requires experimental testing of pathophysiological reasoning, where possible
Historical Examples of Pathophysiologica l
Reasoning Contradicted by Clinical Research

- For decades, physicians prescribed long-term hormone replacement therapy (HRT) for post-menopausal women to reduce their risk of cardiovascular disease.
  - Although much basic science research relating estrogen pathways and cardiovascular physiology supported this practice, it was discontinued in the early 2000s after the landmark Women’s Health Initiative clinical trial found an increased risk of cardiovascular disease and certain cancers among women using HRT.

- Many pediatricians long supported targeting low blood oxygen saturation levels (~85%) for critically ill infants on ventilators to reduce the risk of retinal damage.
  - Although basic science demonstrated the relationship between high oxygen saturation levels and retinal damage, results from the SUPPORT trial published in 2010 found that many more infants died at lower oxygen levels than at higher ones—a much more serious outcome than retinal damage.
The EBCP Approach to Medical Decisions

- Although anecdote, expert opinion, and pathophysiologic reasoning have important places in medical practice, “evidence-based” practice requires the integration of systematic clinical research into clinical decision making.

- As you will learn, there are many reasons that this task is not as simple as it sounds:
  - Sometimes, there is no available research or research involving patients similar to yours
  - Not all patients are the same; most are not “average”
  - Clinical research can convey facts, but not values; just because a treatment may have an effect does not necessarily mean an individual patient should receive that treatment

- However, EBCP proposes that clinicians at least consider clinical research in their decision making.
  - EBCP suggests that knowing what has been demonstrated in clinical research is better than not knowing it—that it is “better to fumble around in the light than in the dark”
Essential Steps of EBCP
Essential Steps of EBCP

- Imagine again the diabetic patient. You are interested in determining which treatment will have the best effect for her.

- Consider what clinical research has to contribute to your decision. You might:
  - Ask a well-defined question (e.g., including a definition for “best effect”)
  - Acquire relevant medical literature to your question
  - Appraise this literature, interpreting and weighing its results
  - Apply this information in making your decision

- These steps constitute the essential steps of EBCP
Essential Steps of EBCP

1. Ask
2. Acquire
3. Appraise
4. Apply

Patient Dilemma
Review: Types of Questions & Types of Medical Literature

- **Background Questions**
  - General knowledge questions
  - Commonly asked by medical & PA students
  - Best answered by *secondary literature* (e.g. textbooks, review articles)
  - **Examples:** How does glipizide work? What are the diagnostic criteria for diabetes?

- **Foreground Questions**
  - Patient-oriented, specific questions
  - Common in clinical practice → **this type of question is the usual focus for applying EBCP techniques**
  - Often best answered by *primary literature*, but systematic reviews & meta-analyses or EBM summaries (e.g. Dyna-Med) may be available
  - **Example:** how does glipizide compare to metformin in the treatment of an overweight patient with the new diagnosis of type 2 diabetes?
Domains & EBCP

- Foreground questions can usually be classified into one of four “domains”:
  - Intervention (treatment or prevention)
  - Diagnosis
  - Prognosis
  - Risk (also referred to as Harm or Etiology or Causation)

- The domain of the question helps us determine the type of research study that will provide the most valid evidence

- Stay tuned for much more information on the topic of question domains in later modules!
Overview of Types of Medical Research Studies
Almost all medical research can be considered either “interventional” or “observational.”

Interventional research (also called “experimental”) requires that the researcher initiate an intervention.

- e.g., In the Women’s Health Initiative clinical trial of hormone replacement therapy for postmenopausal women, women were assigned to groups and researchers provided them with either a regular dose of hormones or a placebo. They then followed these subjects to see whether their intervention had an effect on cardiovascular outcomes.

Observational research requires that the researcher is not involved in administering any intervention.

- e.g., In the Framingham Heart Study, researchers collected data on thousands of residents of Framingham, Massachusetts, and their families. At regular intervals, researchers collected various data, including diet information, cardiovascular imaging, and clinical outcomes, in order to see how these factors were related.
Interventional Research

- In medicine, interventional research is often called a **clinical trial**.
  - Clinical trials are particularly useful to determine the efficacy of therapies used for prevention or treatment.

- They allow the researcher to determine which patients receive an intervention and permit the use of randomization, blinding, and placebo-control.
  - These strategies will be discussed in a future module
  - They help to decrease common sources of error in studies that can lead to wrong conclusions: e.g. **confounding** and **bias**.
  - The abbreviation “RCT” refers to a “randomized controlled trial,” and implies that it was a clinical trial that included random assignment of patients to “interventional” and “control” groups. This is considered by many to be the gold standard in study design for treatment questions.

- Interventional studies are necessarily **prospective**.
  - That is, they require that the study is planned in advance of data collection and analysis. The data in a clinical trial are collected with the purpose of answering a specific clinical question.
Observational Research

- In contrast, observational research can be either prospective or retrospective.
  - **Retrospective** research takes place after data has already been collected. It “looks back” on existing data—for example, information from an electronic medical record or insurance company—to ask and attempt to answer a research question.

- Observational research is particularly useful for:
  - Testing hypotheses using existing data (retrospective analyses, in particular, are quick and inexpensive)
  - Considering questions for which interventional research would be unethical, including most questions in the “Risk” domain (e.g., a study to determine whether a known toxic substance causes birth defects)
  - Answering questions about long-term prognosis (e.g., following a group of patients after chemotherapy and evaluating their long-term comorbidities)
**Basic Types of Observational Research**

*Interventional* research is generally in the form of a clinical trial. However, there are various types of *observational* research study designs:

- **Cross-sectional studies:**
  - Look for associations within a population at one point in time, a “snapshot”
  - Format typically involves a survey or interview +/- physical exam and/or diagnostic testing
  - Can estimate prevalence* (but not incidence* – because you only have information about one time point)

- **Case-control studies:**
  - Start by identifying groups with a specified outcome (e.g., individuals with and without heart disease) and then look backwards in time at possible associated exposures (e.g., daily aspirin use, diet, etc.)
  - Are always retrospective (because the outcomes have already occurred)
  - Generally use an odds ratio* to compare likelihood of exposure in cases (e.g., individuals with heart disease) and controls (e.g., individual without heart disease)

- **Cohort studies**
  - Start by identifying groups with a specified exposure (e.g., individuals using and not using daily aspirin) and then look at associated outcomes (e.g., heart disease)
  - May be prospective (e.g. follow-up visits or surveys moving forwards in time) or retrospective (e.g. use existing data sources from insurance companies or clinic systems that have already been collected)
  - Generally use a relative risk* to compare the likelihood of an outcome in those exposed and unexposed

*Unfamiliar vocabulary will be defined in later modules, e.g. prevalence vs. incidence, odds ratio, relative risk*
Observational Research - terminology

- Before going any further, familiarize yourself with these definitions (cross-sectional, case-control, and cohort). As you progress in your study of EBCP, you will learn more about why various designs are used in various situations.
  - But, first, it is important to be able to simply define and identify these study designs.

- Also, note the use of the terms exposure and outcome, which are commonly used in clinical research.
  - Exposures are generally modifiable.
    - In interventional research, investigators can assign exposures.
    - In observational research, exposures are often self-selected by participants (e.g., choosing to take aspirin), or outside of both participants and researchers’ control (e.g., exposure to pollutants)

- Many observational studies look for an association between an exposure and a specific outcome (e.g., does daily aspirin use reduce the risk of cardiovascular disease?)
Examples of Study Designs
Example: A national survey in January, 2008 shows that the proportion of Americans using at least one prescription drug in the past month is 48%. Among those users, 74% were female.

Note that this study takes place at a single point in time (past month).
Example: Case-Control Study

- Example: A comparison of the smoking history of a group of hospitalized men with lung cancer with the smoking history of a similar group without lung cancer (Doll, 1947).

- This famous study was conducted by Sir Richard Doll in 1947 and helped provide the first evidence of smoking’s relationship to lung cancer.

- Note that it groups by outcome (cases are those with lung cancer; controls are those without*) and then assesses exposure (smoking).

*Note: This is why this design is called “case-control.”
Example: Cohort Study (Prospective)


- Note that this study tests the same hypothesis as Doll’s case-control study. However, it groups the analyzed groups by exposure (smoking) and then looks for outcomes, moving forwards through time.
Example: Cohort Study (Retrospective)

- Comparison of mortality rates of shipyard workers who handled asbestos in 1947 and those who did not.

- Unlike in the previous example, this study uses data that has already been collected for a different purpose.
  - It is retrospective because it “looks back” at events that have already happened (as opposed to the previous study, in which participants are considered in groups and researchers “wait” for outcomes to occur).
  - Often, the data may not have been collected originally in order to answer a research question, so retrospective cohort studies may be considered a type of “data mining” research.
Introduction to Levels of Evidence
Two Core Principles in EBCP*

I. THE BETTER THE RESEARCH EVIDENCE, THE MORE CONFIDENT OUR CLINICAL DECISIONS
(Or... Not all clinical research evidence is created equal)

II. EVIDENCE ALONE IS NEVER SUFFICIENT TO MAKE CLINICAL DECISIONS

This semester, the focus will be on understanding the first principle; next semester we will start applying it to clinical decisions and wrestling with the second principle

*Adapted from a CAPSI lecture by Dr. Mark Wilson - you will see this again!
Levels (Hierarchy) of Evidence: What research can we trust to guide clinical decisions?

1. Systematic Reviews and Meta-analyses
2. Randomized Controlled Trials
3. Cohort studies
4. Case-Control studies
5. Case series
6. Case reports
7. Unsystematic observations
Where can we find the different types of evidence?

A good general approach is to work top-down while also keeping in mind that different questions types are best answered by different types of studies.

Adapted from Supporting Clinical Care: An Institute in Evidence-Based Practice for Medical Librarians. (2010). Evidence Pyramid. http://www.dartmouth.edu/~biomed/institute2010/
Key Points for Module 2

- Evidence-based clinical practice involves acquiring, analyzing, and synthesizing information from clinical experience with the goals and values of particular patients and the best available evidence from scientific research.

- The essential steps of EBCP include **asking** a clinical question, **acquiring** relevant medical literature, **assessing** that literature, and **applying** the information learned from it in clinical practice.

- Research in medicine can be broadly classified into interventional and observational; the three most common types of observational studies are cohort, case-control, and cross-sectional studies.

- Not all research evidence is created equal. The concept of “levels of evidence” can help guide our application of research evidence to patient care.
Please complete the ICON quiz.

Thank you!

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