Evidence-Based Decision Support at the Bedside, What are the Best Resources?

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Immediate Past President of the California Neurology Society (2015-2016)
Past Governor of the ACP Southern CA, Region 2 (2008-2012)
Past President of the LA Neurological Society (2006-2009)
Past President of LA County Med. Association-District 1 (2006-2008)
Medical/Public Historian and Lecturer
Staff Neurologist at SMMC
Staff Rheumatologist at CSMC
Staff Physician at the Klotz SHC at CSUN
Diplomate in Internal Medicine, Rheumatology, Neurology, Headache Medicine, Geriatrics, Sports Medicine, Emergency Medicine, Occupational Medicine, Public Health and General Preventive Medicine via the ABPM, Public Health via the NBPHE and Hypertension
Good Morning and Welcome
Objectives for the Lecture
Objectives

• Augment the participant’s understanding of the terminology involved in a medical literature review and evidence-based medicine.

• Assist the participant in becoming an effective and efficient user of medical literature and how to do a MEDLINE Search.

• Analyze what is involved in an evidence based medicine review.

• Promote what questions are important in the evaluation of a clinical medical study.

• Improve the participant’s skills in discerning what provides solid evidence-based medicine using primary and secondary literature reviews and where to find such information including pre-appraised or summarized evidence in the form of systemic reviews, meta-analyses, guidelines, etc.
No Drug Company Affiliation Relevant to this Lecture
Speakers Bureau for Genzyme on Rare Diseases
I WANT YOU TO TURN OFF YOUR CELL PHONE
Methods of Teaching

- Handout
- Case Presentation
- Lecture
- Post Lecture Quiz
- Question and Answer Period
And Now the Case Presentation
Case Presentation

• Your health care organization is emphasizing the importance of evidence based medicine. Why is this transformation in medicine both important and necessary to the patient, to the physician and to the health care organization?
Answer to Case Presentation

- **Caring for patient requires clinically important information**: Dx, Rx, Prognosis

- **Knowledge deteriorates with time**. Physicians generally practice what they learned in their residency: EBM—life-long, self-directed learning

- **New Evidence often changes Clinical Practice**

- **Prospective learning** from reading journals is important, but not sufficient!

- **Physicians are inundated with medical information**

- **Cost Issues**
So, Let’s Start the Show!!!
Evidence Based Medicine, the New Kid on the Block?
Medicine is a science of uncertainty and an art of probability.

William Osler
“You should randomize till it hurts”

Archie Cochrane*

Source: Cochrane AL. Effectiveness and efficiency: random reflections on health services. London: Nuffield Provincial Hospitals Trust; 1973
The Art of Traditional Medicine
Traditional Medicine

**Traditional medicine** is the sum total of the knowledge, skills, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness.*

*source: World Health Organization, Traditional Medicine: Definitions at the website: [http://www.who.int/medicines/areas/traditional/definitions/en/] on 8/13/17*
Dinosaur Doctors And The Death Of Paternalistic Medicine
"The traditional practice of medicine is a paternalistic affair – the patient goes to the doctor, the doctor tells the patient what to do and the patient does as ordered (or more often, doesn’t do exactly as the doctor ordered). The doctor plays the part of parent. Over the past century, this accepted medical practice did much to foster the “god complex” many doctors are perceived to have to this day."

Claire McClanahan, Dinosaur Doctors and the Death of Paternalistic Medicine 2013
The Practice of Medicine in the 21st Century
“A physician who takes immunity from the medical literature cannot be certain they are providing optimal health care to their patients; such is also the case for a physician who passively accepts all medical research as valid truth.”*

"Never memorize something that you can look up"

Albert Einstein

Source: https://www.quora.com/What-is-the-meaning-of-never-memorize-something-that-you-can-look-up
Life Long Learning

• The hardest conviction to get into the mind of a beginner is that the education upon which he is engaged...a medical course, but a life course, for which the work of a few years under teachers if but a preparation.

Sir William Osler
What is "evidence-based medicine?"
What is Evidence Based Medicine (EBM)?

• Evidence Based Medicine is conscious, specific, reasonable use of modern, best evidence in making decisions about treatment of individual patients.*

In the early 1990s, opinion-based medicine began to give way to evidence-based medicine.

<table>
<thead>
<tr>
<th>Opinion-based medicine</th>
<th>Physician-centered EBM</th>
<th>Patient-centered EBM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relies on memory</td>
<td>Popular since 1992</td>
<td>Emphasize clinical evidence</td>
</tr>
<tr>
<td>Emphasizes experience</td>
<td>Published clinical science</td>
<td>Focus on patient understanding</td>
</tr>
<tr>
<td></td>
<td>Practitioner experience is important</td>
<td>Integrate physician experience with patient values</td>
</tr>
<tr>
<td></td>
<td>Acknowledges patient values</td>
<td></td>
</tr>
</tbody>
</table>

Source: Guggenheim, R, Putting EBM to Work (Easier Said Than Done), Managed Care December 2015 at the website: https://www.managedcaremag.com/issue/2005/December
Some milestones in the history of EBM

James Lind
publishes review & clinical trial in Treatise on Scurvy

Bradford-Hill
publishes Principles of Medical Statistics & MRC trial of streptomycin

900 AD
1780
1840
1937/48
1967
1970's

Al-Rhazi
For I once saved one group by it, while I intentionally neglected another group. By doing that, I wished to reach a conclusion.

Pierre Louis
Develops his “numerical method” and changes blood letting practice in France

Alvan Feinstein
publishes his book Clinical Judgement

Source: http://slideplayer.com/slide/5709736/
Archie Cochrane (1909 – 1988)
British physician & epidemiologist

Pioneer in health services research
His visions are at the heart of Cochrane Collaboration

Founder of the Cochrane Collaboration

• “It is surely a great criticism of our profession that we have not organized a critical summary, by specialty or subspecialty, adapted periodically, of all relevant randomized control trials.”*

Evidence-Based Medicine

What is Evidence-Based Medicine?

“...the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients”

“ It’s about integrating individual clinical expertise and the best external evidence”

philosophical origins – date back to mid-19th century Paris (or possibly earlier)
McMaster highlighted for role in evidence-based medicine

Published: January 31, 2014

David Sackett, Brian Haynes and Gord Guyatt (from left) were featured in 2 important medical journals that praised McMaster faculty as pioneers of evidence-based medicine.

“Evidence-based medicine is the integration of best research evidence with clinical expertise and patient values”

- Dave Sackett
The art of medicine consists of three elements: the disease, the patient and the doctor

~ Hippocrates ~

www.StatusMind.com
The Purpose of EBM

• With appropriate application, it fosters cost-effective and improved health care.

• Its use provides the best possible evidence that the physician can make a judicious choice for the best possible solution and hopefully, optimal health care.

• It is used to avoid major mistakes in the course of treatment and raises the quality of care.

The Purpose of EBM

• Ultimately, the purpose of Evidence Based Medicine is to **save lives and improve the quality of life.**
EBM Misconceptions

Myths
• EBM is useless when there is no good evidence.
• EBM is algorithms that ignore clinical judgment or expertise.
• EBM is just numbers and statistics.

Truths
• Means approximately using the best available evidence to care for patients.
• Clinical judgment must be used in deciding how to apply the evidence.
• EBM is not numbers in a vacuum—the evidence must be individualized to each patient.
I'M MAD AS HELL
AND I'M NOT GOING TO TAKE THIS ANYMORE!

Why EBM in the Real World of Practicing Medicine?

• I have too many patients!
• There are too many questions to address!
• There is too much information out there! I need the simple PEARLS of Medicine.
• Between working a 12 hour day, increasing travel time back and forth to work and a family, where do I find the time to read!
• If I do read, I choose topics that I am familiar with and avoid complex matters.
Why should the Physician choose EBM?

- **Caring for patient requires clinically important information**: Dx, Rx, Prognosis
- **Knowledge deteriorates with time**. Physicians generally practice what they learned in their residency: EBM—life-long, self-directed learning
- **New Evidence often changes Clinical Practice**
- **Prospective learning** from reading journals is important, but not sufficient!
Even when guidelines reflect the evidence they become dated rather quickly

The solid line represents the Kaplan-Meier curve for the Agency for Healthcare Research and Quality (AHRQ) guidelines. The dashed lines represent the 95% confidence interval (JAMA. 2001;286:1461-1467)
Could It Rheumatoid Arthritis???
<table>
<thead>
<tr>
<th>Criteria</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Morning stiffness</td>
<td>Morning stiffness lasting at least 1 hour before maximal improvement</td>
</tr>
<tr>
<td>2. Arthritis of 3 or more joint areas</td>
<td>At least three joint areas simultaneously affected and observed by a physician. The possible areas include the right or left PIP, MCP, wrist, elbow, knee, ankle, and MTP joints.</td>
</tr>
<tr>
<td>3. Arthritis of hand joints</td>
<td>Arthritis in wrist, MCP, or PIP joint</td>
</tr>
<tr>
<td>4. Symmetric arthritis</td>
<td>Simultaneous involvement of the same joint areas on both sides of the body.</td>
</tr>
<tr>
<td>5. Rheumatoid nodules</td>
<td>Subcutaneous nodules over bony prominences, extensor surfaces, or in juxta-articular regions as observed by a physician</td>
</tr>
<tr>
<td>7. Radiographic changes</td>
<td>Radiographic changes typical of rheumatoid arthritis on posteroanterior hand and wrist radiographs showing juxta-articular bone thinning or erosions</td>
</tr>
</tbody>
</table>

For classification purposes, a patient shall be said to have rheumatoid arthritis if he/she has satisfied at least four or these seven criteria. Criteria 1 through 4 must have been present for at least six weeks.

2010 ACR-EULAR classification criteria for rheumatoid arthritis

Target population: Patients who have at least 1 joint with definite clinical synovitis (swelling) with the synovitis not better explained by another disease.

Classification criteria for RA: (score-based algorithm: add score of categories A - D; a score of ≥6/10 is needed for classification of a patient as having definite RA).

The metacarpophalangeal joints, proximal interphalangeal joints, the interphalangeal joint of the thumb, second through fifth metatarsophalangeal joint and wrist as small joints, and shoulders, elbows, hip joints, knees, and ankles as large joints.

A. Joint involvement

<table>
<thead>
<tr>
<th>Number of Joints</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 large joint</td>
<td>0</td>
</tr>
<tr>
<td>2-10 large joints</td>
<td>1</td>
</tr>
<tr>
<td>1-3 small joints (with or without involvement of large joints)</td>
<td>2</td>
</tr>
<tr>
<td>4-10 small joints (with or without involvement of large joints)</td>
<td>3</td>
</tr>
<tr>
<td>&gt;10 joints (at least 1 small joint)</td>
<td>5</td>
</tr>
</tbody>
</table>

B. Serology: (at least 1 test result is needed for classification)

<table>
<thead>
<tr>
<th>Test Result</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative RF and negative ACPA</td>
<td>0</td>
</tr>
<tr>
<td>Low-positive RF or low-positive ACPA</td>
<td>2</td>
</tr>
<tr>
<td>High-positive RF or high-positive ACPA</td>
<td>3</td>
</tr>
</tbody>
</table>

C. Acute-phase reactants: (at least 1 test result is needed for classification)

<table>
<thead>
<tr>
<th>Test Result</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal CRP and normal ESR</td>
<td>0</td>
</tr>
<tr>
<td>Abnormal CRP or abnormal ESR</td>
<td>1</td>
</tr>
</tbody>
</table>

D. Duration of symptoms

<table>
<thead>
<tr>
<th>Duration</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6 weeks</td>
<td>0</td>
</tr>
<tr>
<td>≥6 weeks</td>
<td>1</td>
</tr>
</tbody>
</table>
COULD IT BE LUPUS?

by Lupus Foundation of America
<table>
<thead>
<tr>
<th><strong>1997 ACR criteria</strong></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malar rash</td>
<td>Fixed erythema, flat or raised, over the malar eminences</td>
</tr>
<tr>
<td>Discoid rash</td>
<td>Erythematous circular raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur</td>
</tr>
<tr>
<td>Photosensitivity</td>
<td>Exposure to ultraviolet light causes rash</td>
</tr>
<tr>
<td>Oral ulcers</td>
<td>Includes oral and nasopharyngeal ulcers, observed by physician</td>
</tr>
<tr>
<td>Arthritis</td>
<td>Nonerosive arthritis of two or more peripheral joints, with tenderness, swelling, or effusion</td>
</tr>
<tr>
<td>Serositis</td>
<td>Pleuritis or pericarditis documented by ECG or rub or evidence of effusion</td>
</tr>
<tr>
<td>Renal disorder</td>
<td>Proteinuria &gt;0.5 g/d or 3+, or cellular casts</td>
</tr>
<tr>
<td>Neurologic disorder</td>
<td>Seizures or psychosis without other causes</td>
</tr>
<tr>
<td>Hematologic disorder</td>
<td>Hemolytic anemia or leukopenia (&lt;4000/L) or lymphopenia (&lt;1500/L) or thrombocytopenia (&lt;100,000/L) in the absence of offending drugs</td>
</tr>
<tr>
<td>Immunologic disorder</td>
<td>Anti-dsDNA, anti-Sm, and/or anti-phospholipid</td>
</tr>
<tr>
<td>Antinuclear antibodies</td>
<td>An abnormal titer of ANA by immunofluorescence or an equivalent assay at any point in time in the absence of drugs known to induce ANAs</td>
</tr>
</tbody>
</table>

If 4 of these criteria, well documented, are present at any time in a patient's history, the diagnosis is likely to be SLE.
2012 SLICC Classification Criteria for Systemic Lupus Erythematosus

Biopsy proven Lupus Nephritis and ANA or anti-DNA

**Clinical**
- Acute cutaneous LE
- Chronic cutaneous LE
- Oral ulcer
- Alopecia
- Synovitis
- Serositis
- Renal
- Neurologic
- Hemolytic anemia
- Leucopenia/lymphopenia
- Thrombocytopenia

**Immunologic**
- ANA
- Anti-dsDNA
- Anti-Sm
- aPL antibodies
- Low complement
- Direct Coomb’s test

**At least 4 Criteria**
(1 Needs to be IMMUNOLOGIC)

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2015 ACR/ SLICC Revised Criteria for Systemic Lupus Erythematosus

- Acute Cutaneous LE
  - Malar rash (2)
  - SCLE rash (1)
  - Urticarial vasculitis (1)
  - Photosensitivity (1)
- Discoid LE (1)
- Alopecia (1)
- Oral ulcers (1)
- Joint disease (1)
- Serositis (1)
- Psychosis or seizures or acute confusion state (1)

- Kidney
  - Proteinuria or casts (1)
  - Biopsy proven LN (2)
- Hemolytic anemia (1)
- Thrombocytopenia (1)
- Leucopenia/ lymphopenia (1)
- Low titer ANA (1)
- High titer ANA – homo/ rim (2)
  - Positive ANTI-DSDNA (2)
  - Positive ANTI-SM (2)
  - APL antibodies (1)
  - Low complement (1)
Why should the Physician choose EBM continued?

- **Physicians are inundated** with medical information:
  - Thousands of Biomedical Journals on Medline
  - Millions of Journal Articles
  - Lag Period between publication of research findings and implementation in clinical practice
  - All studies are not created equal in design or interpretation
  - Adding expert synthesis and analysis can help the overburdened physician
Even if the evidence exists, it is becoming increasingly more difficult for providers to find it.

>300,000 controlled clinical trials

>150,000 articles published/month

20,000 biomedical journals

Source: Guggenheim, R, Putting EBM to Work (Easier Said Than Done), Managed Care December 2015 at the website: https://www.managedcaremag.com/issue/2005/December
Getting information off the Internet is like taking a drink from a fire hydrant.

— Mitchell Kapor

Source: https://www.linkedin.com/pulse/6-things-formula-one-can-teach-you-building-social-media-ali-bullock
Exponential growth of the medical literature from 1946 to 2015

Time-poor clinician suffering from Information Overload

Source: https://www.slideshare.net/DrSUHASINIKANYADI/evidence-based-medicine-43822003
Why EBM?

What is the need?

- **Cost**
- Delay of "bench-to-bedside" research
- Managing the primary literature
- Counter misleading marketing
- Dealing with conflicting results

increasing pressure to

- demonstrate effectiveness of interventions
- utilize the most cost effective measures

How do you know what really works or is the most cost effective?
Why EBM in the Real World of Practicing Medicine?

• I have too many patients!
• There are too many questions to address!
• There is too much information out there! I need the simple PEARLS of Medicine.
• Between working a 12 hour day, increasing travel time back and forth to work and a family, where do I find the time to read!
• If I do read, I choose topics that I am familiar with and avoid complex matters.
What does Evidence Based Medicine involve?

- Evidence-based medicine includes three key components:
  1) Research-based evidence,
  2) Clinical expertise (i.e., the clinician’s accumulated experience, knowledge, and clinical skills),
  3) The patient’s values and preferences.
Research-Based Evidence

- **Best research evidence** = clinically relevant research
  - from basic sciences of medicine
  - from patient-centered clinical research focusing the following:
    - the accuracy and precision of diagnostic tests (including the clinical examination)
    - the power of prognostic markers
    - the efficacy and safety of therapeutic, rehabilitative, and preventive strategies.
ACCURACY VERSUS PRECISION

**Accuracy**
- Indicates how close a measurement is to the correct or accepted value.
- Your measurement will be close to the standard measurement.
- Accuracy is not dependent on precision.

**Precision**
- Indicates the closeness of two or more measurements to each other.
- Your measurement will be similar every time you measure.
- Precision is not dependent on accuracy.

Source: https://sites.google.com/a/apaches.k12.in.us/mr-evans-science-website/accuracy-vs-precision
Clinical Expertise

• Clinical Expertise:

• the ability to use clinical skill and past experience

• to rapidly identify each patient's unique health state and diagnosis,

• their individual risks and benefits of potential interventions,

• their personal values and expectations.
Paternalistic Approach vs Patient-Centered Approach

Tell me your thoughts...

Do What I Tell You
Patient Values and Preferences

• *Patient values and preferences:*
  - the unique preferences, concerns and expectations each patient brings to a clinical encounter
  - the above needs be integrated into clinical decisions if they are germane and serve the patient

• *Patient preferences*
  - their individual clinical state and the clinical setting.
Five Ways that EBM adds Value to Health Systems

1) Helps clinicians stay current on standardized, evidence base protocols.

2) Uses near real-time data to make care decision.

3) Improves transparency, accountability and value.

4) Improves quality of care.

5) Improves outcomes.
Limitations of EBM

Time consuming
Requires access to medical literature
Requires some knowledge of statistics
Publication bias
Conflicts of interest

Source: https://www.youtube.com/watch?v=P-G2veeYC1Q
The Transition from Traditional to Evidence Based Medicine
The Transition to Evidence Based Medicine will require physicians...

- Physicians to change how they were taught to diagnose and treat patients: (i.e., from internship and residency).

- It will take time for providers who are trying to keep up with their workloads to treat patients the best that they know how with a new model of care delivery and use it efficiently.
Requirements for EBM
What do you need to know about EBM?

- Willingness to change
- Working knowledge of the English language
- Familiarity with the use of computers, cell phones and electronic health records
- The ability to search medical literature
- Basic skills in the interpretation of epidemiological and statistical results
The Evidence Based Process

Source: http://www.quotemaster.org/evidence+based+medicine
5 A's
Acquire the best evidence
Ask clinical questions
Appraise the evidence
Apply evidence to patient care
Assess your patient

Source: http://mcw.libguides.com/EBM
Step 1: Ask the Clinical Question
Serve una svolta decisa.

Asking a Clinical Question

• Begins with a tight, explicit formulation of the question.

• **PICO**
  - What is the relevant *patient* population?
  - What *intervention* is being considered?
  - What is the *comparison* intervention or patient population?
  - What *outcomes* are of interest?
**PICO Formula**

**P** - Patient, population or problem: What are the most important characteristics of the patient and their health status?

**I** - Intervention/Exposure: What main intervention are you considering (medical, surgical, preventative)?

**C** - Comparison: What are the alternative benchmark or gold standards being considered, if any?

**O** - Outcome: What is the estimated likelihood of a clinical outcome attributable to a specific disease, condition or injury?

Components of Clinical Questions

Patient/Population
- In patients with acute MI
- In women with suspected coronary disease
- In postmenopausal women

Intervention/Exposure
- does early treatment with a statin
- what is the accuracy of exercise ECHO
- does hormone replacement therapy

Comparison
- compared to placebo
- compared to exercise ECG
- compared to no HRT

Outcome
- decrease cardiovascular mortality?
- for diagnosing significant CAD?
- increase the risk of breast cancer?
<table>
<thead>
<tr>
<th>Patient or Problem</th>
<th>Intervention</th>
<th>Comparison intervention</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Describe a group of patients similar to your own</td>
<td>What intervention are you considering</td>
<td>What is the main alternative to the intervention</td>
<td>What do you hope to accomplish with the intervention</td>
</tr>
<tr>
<td>“In elderly patients with congestive heart failure ...”</td>
<td>…does treatment with spirinolactone ...</td>
<td>…when compared with standard therapy alone...</td>
<td>…lead to a decrease in hospitalization ”</td>
</tr>
</tbody>
</table>

Source: http://www.cebm.net/makes-good-clinical-question-fellows-view/
Step 2: Acquire the Best Evidence
Sources of Evidence

• Primary sources
  – Based on experiments and published research

• Secondary sources
  – Systematic reviews
  – Clinical guidelines
  – Journals of secondary publication e.g. Evidence Based Medicine
Apps for Evidence Based Medicine
Apps in Medicine

- Information Management, Time Management and HR Management and Access
- Communication and Consulting
- **Medical References and Information Gathering**
- **Clinical Decision-Making**
- Patient Monitoring
- Medical Education and Training
Apps to Consider for EBM

• **Epocrates**: Drug and Medical Reference
• **PEPID**: Clinical Decision Support Reference targeted to ER physicians
• **UptoDate**: Medical Reference
• **Doximity**: Social Networking Site for Physicians
• **Read by QxMD**: Centralizes all your Medical Literature and Journals
• **NEJM This Week**: Medical Reference
• **Isabel**: Medical Reference
• **Figure 1**: View and Share Medical Images with other Physicians
• **DynaMed Mobile**: Medical Reference
• **Medscape**: Medical Reference
### Table 3

**Free Evidence-Based Databases**

<table>
<thead>
<tr>
<th>Database</th>
<th>URL</th>
</tr>
</thead>
<tbody>
<tr>
<td>PubMed</td>
<td><a href="http://www.pubmed.com">www.pubmed.com</a></td>
</tr>
<tr>
<td>National Guideline Clearinghouse</td>
<td><a href="http://www.guideline.gov">www.guideline.gov</a></td>
</tr>
<tr>
<td>TRIP Database</td>
<td><a href="http://www.tripdatabase.com/index.html">www.tripdatabase.com/index.html</a></td>
</tr>
</tbody>
</table>

**Subscription Evidence-Based Medicine Databases**

<table>
<thead>
<tr>
<th>Database</th>
<th>URL</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACP Journal Club</td>
<td><a href="http://www.acpjhc.org">www.acpjhc.org</a></td>
</tr>
<tr>
<td>ACP Medicine</td>
<td><a href="http://www.acpmedicine.com">www.acpmedicine.com</a></td>
</tr>
<tr>
<td>Clinical Evidence</td>
<td><a href="http://clinicaleducation.bmj.com">http://clinicaleducation.bmj.com</a></td>
</tr>
<tr>
<td>Clinical Pharmacology</td>
<td><a href="http://www.clinicalpharmacology.com">www.clinicalpharmacology.com</a></td>
</tr>
<tr>
<td>Cochrane Library</td>
<td><a href="http://www.cochrane.org">www.cochrane.org</a></td>
</tr>
<tr>
<td>First Consult</td>
<td><a href="http://www.firstconsult.com">www.firstconsult.com</a></td>
</tr>
<tr>
<td>Essential Evidence Plus</td>
<td><a href="http://www.essentialmedicineplus.com">www.essentialmedicineplus.com</a></td>
</tr>
<tr>
<td>PIER: Physicians’ Information and Education Resource</td>
<td><a href="http://pier.acponline.org">http://pier.acponline.org</a></td>
</tr>
<tr>
<td>UpToDate</td>
<td><a href="http://www.uptodate.com">www.uptodate.com</a></td>
</tr>
</tbody>
</table>

*Source: Albrecht, S., Evidence-Based Medicine in Pharmacy Practice, *US Pharm.* 2009;34(10):HS14-HS18*
Growth in PubMed
<table>
<thead>
<tr>
<th>Type of sources</th>
<th>Examples</th>
<th>Comments</th>
<th>Funding source</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary sources</strong></td>
<td>PubMed</td>
<td>Article searches are needed to find answers to questions. May be difficult to use at the point of care in a busy practice. Workflow reminders to look up this information at the end of each day promote lifelong learning.</td>
<td>Federal government</td>
</tr>
<tr>
<td><strong>Pharmacotherapy</strong></td>
<td>Lexicomp, ePocrates</td>
<td>Practical information about medications such as indications, dosage, adverse reactions, and drug interactions.</td>
<td>Advertising, subscription, data sharing</td>
</tr>
<tr>
<td><strong>Medical calculators</strong></td>
<td>MDCalc</td>
<td>Tools to calculate cardiovascular risk, medication dosage adjustment in renal insufficiency, sodium replacement in hyponatremia, more.</td>
<td>Unclear</td>
</tr>
<tr>
<td><strong>Guidelines databases</strong></td>
<td>National Guideline Clearing House, USPSTF</td>
<td>A searchable collection of guidelines developed by various government-funded or professional societies which allow side-by-side comparisons and ratings for strength of evidence for individual recommendations.</td>
<td>Federal government</td>
</tr>
<tr>
<td><strong>Systematic reviews of medical evidence</strong></td>
<td>Cochrane Collaboration, Centre for Reviews and Dissemination</td>
<td>Provide high-quality up-to-date syntheses of research evidence. Robust and unbiased information to help clinicians make decisions.</td>
<td>Subscription, university</td>
</tr>
<tr>
<td><strong>Evidence search tools</strong></td>
<td>PubMed</td>
<td>Clinical queries provide busy clinicians fast access to reliable clinical studies using preset research methodology filters. Designed to find those few “good” articles that can help us make decisions at the point of care.</td>
<td>Federal government</td>
</tr>
<tr>
<td><strong>Online textbooks</strong></td>
<td>Access Medicine, Harrison’s Principles of Internal Medicine</td>
<td>Easily accessible and updated more frequently than their print versions. Additional features such as multimedia materials, search capabilities, and ability to share notes turn these into excellent resources, especially for questions that often come up when working with residents or students.</td>
<td>Subscription</td>
</tr>
<tr>
<td><strong>Online texts and summary sources</strong></td>
<td>Dynamed, UpToDate, Clinical Evidence</td>
<td>Fast clinical answers at the point of care. Can be accessed from desktop or mobile devices.</td>
<td>Subscription</td>
</tr>
<tr>
<td><strong>Internet search</strong></td>
<td>Wikipedia, Google</td>
<td>An Internet search not directly in a medical reference can provide more information including that from patients and industry, but reliability and validity can limit use without discrimination of results. Google searches can replicate findings from summary sources in speed and accuracy.</td>
<td>Donations (Wikipedia), advertising (Google)</td>
</tr>
<tr>
<td>Resource</td>
<td>Cost</td>
<td>CME credit</td>
<td>Add-on features</td>
</tr>
<tr>
<td>--------------------</td>
<td>----------------------------------------------------------------------</td>
<td>------------</td>
<td>---------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Clinical Evidence</strong></td>
<td>$36 for 48 hours of access for 1 review</td>
<td>No</td>
<td>Large major reviews of conditions and treatments with graded evidence</td>
</tr>
<tr>
<td></td>
<td>$53 for 30 days of viewing all content</td>
<td></td>
<td>Drug and safety alerts</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Links to full-text major guidelines</td>
</tr>
<tr>
<td><strong>Dynamed</strong></td>
<td>Physicians: $395/year Residency: $150/year Students: $100/year</td>
<td>Yes</td>
<td>Drug database update alerts</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Links to articles</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Practice-changing updates</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Electronic health record integration</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Patient information</td>
</tr>
<tr>
<td><strong>Evidence Essentials</strong></td>
<td>$85/year</td>
<td>Yes</td>
<td>Medical calculators</td>
</tr>
<tr>
<td><strong>First Consult</strong></td>
<td>Based on packages, eg, $499 for internal medicine (8 journals and 11 books), $998 for extended internal medicine (45 journals and 23 books)</td>
<td>Yes</td>
<td>White papers such as “Best time management tips for physicians”</td>
</tr>
<tr>
<td><strong>Medscape</strong></td>
<td>Free with registration</td>
<td>Yes</td>
<td>Drug database&lt;br&gt;Patient information&lt;br&gt;Pill identifier&lt;br&gt;Visual images and videos</td>
</tr>
<tr>
<td><strong>UpToDate</strong></td>
<td>Physicians: $499/year, $53 for a 30-day recurring subscription Residency, fellows, and students: $199/year, $19 for a 30-day recurring subscription</td>
<td>Yes</td>
<td>Drug database&lt;br&gt;Update alerts&lt;br&gt;Links to articles&lt;br&gt;Practice-changing updates&lt;br&gt;Electronic health record integration&lt;br&gt;Patient information</td>
</tr>
</tbody>
</table>
Examples of Hierarchies

Pyramid of Evidence, Medicine

Source:
https://www.slideshare.net/kpadron_libraries/evidence-based-practice-8412826
Types of Studies

Clinical Practice Guideline: Recommendations for clinicians based on a systematic review of evidence.

Meta-Analysis: Combines the results of studies using quantitative methods to statistically estimate the effects of proposed interventions.

Systematic Review: Appraised summary of all the research that addresses a specific clinical question.

Randomized Controlled Trials: A randomized group of patients are assigned to an experimental group and a control group. These groups are followed up on for the variables/outcomes of interest.

Cohort Study: Identifies two groups (cohorts) of patients, one which did receive the exposure of interest, and one which did not. Follows the cohorts forward for the outcome of interest.

Case-Control Study: Identifies patients who have the outcome of interest (cases) and control patients without the same outcome and looks for exposure of interest.

Case Report/Case Series/Expert Opinion: Descriptive study of a single case or series of cases with no research design or generalized information found in textbooks, encyclopedias, etc.

Source: http://libguides.winona.edu/c.php?g=11614&p=81584
<table>
<thead>
<tr>
<th>Past</th>
<th>Present</th>
<th>Future</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cross-sectional study</td>
<td>Case-control study</td>
<td>Prospective Cohort Study</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clinical Trial</td>
</tr>
</tbody>
</table>

Source: https://med.libretexts.org/TextMaps/Map3A_Intermediate_Nutrition_(Lindshield)/13A_Nutrition_Basics/143A_Human_Intervention_Studies2F2FClinical_Trials
**Observational studies**

**Case control**

- Exposed to risk factor
  - Yes
  - No

  _______ Time _______

- Diseased
- Not diseased

**Questions**
- Risk factors

**Measures**
- Odds ratio

**Cohort**

- Sample of people
  - Exposed to risk factor
    - Yes
    - No
  - Not exposed
    - Yes
    - No

  _______ Time _______

**Questions**
- Incidence
- Risk factors
- Prognosis

**Measures**
- Incidence
- Relative risk

Experimental studies

Randomized controlled trial

Sample of patients

- Treated
- Control

Improved
- Yes
- No

Randomization

- Yes
- No

Questions
- Effects of treatment

Measures
- Outcome rates
- Relative risk
- Number needed to treat
- Odds ratio
- Hazard ratio

<table>
<thead>
<tr>
<th>Type of Study</th>
<th>Pro</th>
<th>Con</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Practice Guideline</strong></td>
<td>Authoritative and explicit recommendations based on critical appraisal of current research</td>
<td>Studies on which guidelines are based may be flawed; Overarching guidelines may not be best for individual patients</td>
</tr>
<tr>
<td><em>Recommendations for clinicians based on a systematic review of evidence</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Meta-Analysis/Systematic Reviews</strong></td>
<td>Comprehensive review of studies with highest level of evidence</td>
<td>Difficulty accessing all the articles necessary; M-A: publication bias (studies showing little/no effect are not included)</td>
</tr>
<tr>
<td><em>Synthesis of literature systematically searched for, appraised and summarized on a specific topic</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Randomized Controlled Trial (RCT)</strong></td>
<td>Unbiased distribution of confounders; Blinding likely; Randomization facilitates statistical analysis</td>
<td>Expensive: time and money; Volunteer bias; Can be ethically problematic</td>
</tr>
<tr>
<td><em>Experimental study that uses randomization to assign subjects to a treatment or control group</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Nonrandomized Controlled Trial</strong></td>
<td>More control over the study participants may increase the effectiveness of intervention</td>
<td>Greater risk of selection bias; Greater potential for confounders affecting association between exposure and outcome</td>
</tr>
<tr>
<td><em>A type of quasi-experimental design that does not use randomization to divide subjects</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cohort Study</strong></td>
<td>Ethically safe; Eligibility criteria and outcome assessments can be standardized; Administratively easier/cheaper than RCT</td>
<td>Exposure may be linked to hidden confounder; Blinding is difficult; Randomization not present</td>
</tr>
<tr>
<td><em>Observational study of 2 groups, 1 with exposure of interest 1 without, followed for outcome</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Case Control Study</strong></td>
<td>Quick/cheap; Useful when the outcome is rare; Good at estimating the odds of developing a condition</td>
<td>Reliance on records to determine exposure; Confounders; Selection of control group is difficult; Potential selection bias</td>
</tr>
<tr>
<td><em>Observational study of 2 groups, 1 with outcome of interest 1 without, looks for exposure</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Case Report/Series/Expert Opinion</strong></td>
<td>Easy to understand; Accessible; Provide the basics/background information</td>
<td>No control group so no statistical validity</td>
</tr>
<tr>
<td><em>Descriptive study of a single case or series of cases, generalized info – no research design</em></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sources consulted:
## Identifying the Best Study

<table>
<thead>
<tr>
<th>Type of Question</th>
<th>Suggested best type of Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy</td>
<td>RCT &gt; cohort &gt; case control &gt; case series</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Prospective, blind comparison to a gold standard</td>
</tr>
<tr>
<td>Etiology/Harm</td>
<td>RCT &gt; cohort &gt; case control &gt; case series</td>
</tr>
<tr>
<td>Prognosis</td>
<td>Cohort study &gt; case control &gt; case series</td>
</tr>
<tr>
<td>Prevention</td>
<td>RCT &gt; cohort study &gt; case control &gt; case series</td>
</tr>
<tr>
<td>Clinical Exam</td>
<td>Prospective, blind comparison to gold standard</td>
</tr>
<tr>
<td>Cost</td>
<td>Economic analysis</td>
</tr>
</tbody>
</table>

Source: https://www.slideshare.net/DrSUHASINIKANYADI/evidence-based-medicine-43822003
The image depicts a hierarchy of evidence levels in research. The highest level of evidence is represented by **RCTs** (Randomized Clinical Trials), followed by cohort studies, case-controlled studies, case series, and case report or expert opinion. This pyramid illustrates the strength of evidence, with RCTs being the most robust and case report or expert opinion being the least robust. The source of this diagram is provided at the bottom of the image, linking to a website for evidence-based treatment options.
Levels of Evidence

- Level 1: Evidence in Level I is considered the gold standard of medical knowledge because it comes from randomized controlled clinical trials (RCTs).
- Level 2: Evidence from controlled trials without randomization
- Level 3: Evidence from cohort or case-controlled analytic studies
- Level 4: Evidence from multiple time series i.e. observational studies
- Level 5: Opinions of respected authorities based on medical experience
- Level 6: Evidence based on personal experience (anecdote)
Step 3: Appraise the Evidence
Step 3: Appraise the Evidence

• Physicians need the skills to critically evaluate research.
• The focus of critical appraisal is judging the following:
  ➢ Internal Validity
  ➢ Generalizability (External Validity)
Source: Fletcher RH et al, Clinical Epidemiology: The Essentials, 4th ed, Lippincott Williams & Wilkins, Philadelphia 2005
Internal Validity

- Concerns the accuracy of measurement within the study

- Can be threatened by
  - Biases
  - Confounding
  - History: large scale events that change participants’ attitudes or behavior (e.g., recession)
  - Maturation: participants change over time, e.g., growth, fatigue etc.
  - Repeated Testing: participants get wise to the study and remember the test questions
  - Compensatory rivalry/resentful demoralization: Control participants work extra hard to prove themselves or withdraw because not getting treatment
  - Diffusion: treatment effects spread from treatment group to control group
Internal Validity

• Refers to the question of whether the results of clinical research are correct.

• Threats to Internal Validity

  ➢ Bias
  ➢ Confounding
  ➢ Chance
Errors in epidemiological studies

- Random error (chance)
- Systematic error (bias)

Source:
https://wiki.ecdc.europa.eu/fem/w/wiki/bias
Bias

• Definition: Any systematic error that can produce a misleading impression of the true effect.

• **RCTs are done to reduce bias.**
Potential Sources of Bias

• Failure to conceal random assignment to those enrolling study subjects
• Failure to blind relevant individuals
• Loss to follow up (missing outcome data)
• Failure to adhere to assigned intervention
• Stopping early for benefit
• Preferentially publishing small (underpowered) studies with statistically significant results (publication bias)
Bias Can occur in any Stage in Research

- Literature Review
- Study Design
- Study Execution
- Data Collection
- Analysis
- Interpretation of Results
- Publication
• One major problem with most types of research is **bias**.
  
  - **Experimenter bias** (is the tendency for the researcher to distort the procedures or results of an experiment, based on the expected outcome of the study).
  
  - **Subject bias** (is the tendency for the subject to distort or perform in a manner that is out of the usual and may distort the outcome of the study. Sometimes this is called the *Hawthorne Effect*).
  
  - **Bias** can be controlled through the use of:
    
    • **Blinding** procedures are used to conceal the hypotheses of the experiment from the subject (**single blind**) or from the subject and experimenter (**double blind**) study.
DOUBLE BLIND

Patients
Unaware of the test being conducted.

Test Pills placebo

Control Pills regular

Doctor
Unaware of the test being conducted.

Source:
Common Biases

- **Selection bias**: one relevant group in the population (e.g. cases positive for predictor variable) has a higher probability of being included in the sample.
- **Ascertainment**: bias in asking questions or offering tests of one group over another.
- **Information**: bias from erroneously classifying people in exposure/outcome categories.
- **Adjudication**: bias in determining if the treatment was helpful due to partial or inadequate blinding.
- **Recall/Response**: bias associated with inaccurate recall of exposure or representation of true exposure (self-report).
- **Experimenter/Interviewer bias**: Differential treatment of participants in treatment and control groups.
- **Publication**: the tendency to publish only “positive” or “significant” findings.

Source: https://www.slideshare.net/pbbarlow1/comparing-research-designs-handout-version
Confounding—a form of Bias

• Is the result of failure to account for a risk factor other than the one related to the exposure.

• A confounder
  ➢ must be a risk factor
  ➢ must be associated with the exposure
  ➢ must not be an intermediate step in the causal pathway between the exposure and disease outcome.
Confounding

Source: https://www.healthknowledge.org.uk/e-learning/epidemiology/practitioners/chance-bias-confounding
Strategies to Reduce Confounding

• Randomization
• Restriction of study to individuals with confounding factors
• Matching to aim for equal distribution of confounding
Chance

• Is random error, inherent in all observations
• The probability of chance producing erroneous results can be minimized by a large number of patients

- **P-value**: defines the probability that if the null hypothesis were true, the study would find a difference as large, or larger than the one found.
- **Confidence Intervals**: a range of values so defined that there is a specified probability that the value of a parameter lies within it.
External Validity

- The ability to generalize the findings of your study to the relevant population.

- Threatened by
  - Bias
  - Confounding
  - Non-experimental design (i.e. case-control vs. RCT)
  - Lack of randomization

- External validity is the strongest when a true experimental design is used.
External Validity

• Refers to the question of whether the results of the study apply to patients outside of the study (a specific patient or population) considered by the EBM physician.

• Are the results generalizable?

• Doing a Subgroup Analyses

• Potential Problems
  ➢ Reporting Bias
  ➢ Multiple Comparisons
  ➢ Lower Statistical Power
Step 4: Apply the Evidence
Step 4: Applying the Evidence in Practice

- Often, there is a gap between recommendations of the best available evidence and actual clinical practice.
- There may be cogent reasons for this. (see the next slide)
- EBM is not intended to replace clinical judgment.
Reasons for a Gap

• Uncertainty whether the results of larger studies apply to individual patients
• Lack of awareness or misunderstanding of the evidence
• Failure to organize care in a way that foster the use of evidence
Step 5: Assess Your Performance
Assess Your Performance

• Assess the patient and the problem to determine the pertinent issues which may include differential diagnosis, treatment decisions, or prognosis.
Assess Your Performance: An Evaluation

• Were you able to formulate a focused question?
• Were you able to devise a precise search strategy for locating the evidence?
• Did you use the most appropriate resource?
• Were the more pertinent resources like guidelines available to you?
• Did the evidence work in this patient?
• You should document the outcomes of the application of evidence and based on his own experience.
• May be used for future management protocols.
Assess Your Performance

• Identify barriers and facilitators to this change.
• Identify a strategy to implement this change, targeted to the barriers that were identified.
• Check and audit the diagnostic, therapeutic or other EBM performances including its impact on clinical outcomes.
• Sustainability of this change

In Summary
In Summary, Evidence Base Medicine

• EBM not an exact science, but a science of probability.
• It helps clinicians stay current on standardized, evidence-based protocols.
• It uses real-time data to make care decisions.
• It improves transparency, accountability, and value.
• It improves quality of care.
• It improves outcomes all around.
• By adopting the principles of EBM, it will be possible to maximize the benefits of scientific research for patient care.
• Albrecht, S., Evidence-Based Medicine in Pharmacy Practice, *US Pharm.* 2009;34(10):HS14-HS18


• Cochrane AL. Effectiveness and efficiency: random reflections on health services. London: Nuffield Provincial Hospitals Trust; 1973


• Kim, S et al., Searching for answers to clinical questions using Google versus evidence-based summary resources: a randomized controlled crossover study, *Acad Med* 2014; 89:940-943.


Smith, Richard et al., Evidence based medicine—an oral history, BMJ 2014;348:g371


Post Lecture Question #1

All of the following are key components of evidence based medicine except for which of the following?

a) Patient’s Values and Preferences

b) What Medical School that the Physician attended

c) Clinical Expertise

d) Researched-based Evidence
Secondary, pre-appraised, filtered studies would included which of the following?

a. Meta-Analyses and Consensus Guidelines
b. Randomized Controlled Studies and Consensus Guidelines
c. Cohort and Case Control Studies
d. Editorials and Expert Opinions
Post Lecture Quiz Question #3

In the level of evidence pyramid, what is considered the golden standard?

a. Case Control Studies  
b. Cohort Studies  
c. Randomized Control Trials  
d. Observational Studies
Post Lecture Quiz Question #4

All of the following are purposes for EBM except for which of the following?

a. Cost-effective
b. Improves quality of care
c. Assists in avoiding medical mistakes in treatment
d. Reduces malpractice cases
e. Replaces the physician’s decision with artificial intelligence
f. Enables the physician the make a prudent decision in optimal patient care
Post Lecture Quiz Question #5

• What do the 5 A’s stand for in Evidence Based Medicine?
Answers to Post Lecture Quiz Questions

1. b
2. a-Meta-Analyses and Consensus Guidelines
3. c-Randomized Control Studies
4. e
5. Ask, Acquire, Appraise, Apply and Assess
Question and Answer Period
That’s All Folks. As Chihuahuas, we advocate for the ADACA: All Dog Affordable Care Act—Donald Trump are you listening???
Thank you
The End