

Teaching Evidence-Based Medicine A short syllabus for neurology resident

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Objective: After completion of this course, the resident will have an understanding of evidence-based medicine. They will be able to formulate a clinical question, perform a literature search to answer the question; develop a 2x2 table; understand the basic statistics involved; understand and be able to describe study designs, their relative merits and difficulties; and to be able to do this on a daily basis during their training and practice.

Required Textbook:

Sackett, D.L., Straus, S., Richardson, W.S., Rosenberg, W., Haynes, R.B. Evidence-based Medicine. How to Practice and To Teach EBM. London: Churchill Livingstone, 2000.

Website: Centre for Evidence Based Medicine. <http://cebm.jr2.ox.ac.uk/>

Week 1

Descriptions: Introduction to Evidence-Based Medicine (EBM). Explore the reasons as to why we should practice EBM based upon the introduction and chapter one of Sackett's book.

Preparation: read the first two chapters of Sackett's book. Have enough copies of the text to distribute to the residents. Bring in examples of EBM. Suggested examples:

- Practice parameter
- ACP Journal Club
- EBM user articles from JAMA

Learn how to formulate a question.

A clinical question is composed of a population, an event or transaction, and an outcome measure. Most clinical questions also require a comparison to an acknowledged gold standard to the event or transaction. A clinical question can be developed from any patient encounter and they are useful tools to expand and to update clinical knowledge.

In patients with suspected carpal tunnel syndrome, is quantitative sensory testing as accurate as conventional nerve conduction studies?			
Closed head injury, with GCS > 13	clinical examination	MRI	morbidity due to surgically treatable lesions
In patients with a closed head injury and a GCS > 13, is the clinical examination as sensitive as MRI in reducing mortality due to surgically treatable lesions?			
Alzheimer's disease	Special care units	conventional nursing home facility	quality of life/ economic analysis
In patients with Alzheimer's disease, do special care units provide a better quality of life than conventional nursing home facilities? or In patients with Alzheimer's disease, are special care units more cost effective than conventional nursing home facilities?			
Grade one astrocytoma	chemotherapy	(radiation therapy)	prognosis
In patients with newly diagnosed grade one astrocytoma, does treatment with chemotherapy improve the prognosis? or In patients with newly diagnosed grade one astrocytoma, does treatment with chemotherapy improve the prognosis when compared to radiation therapy?			

The first 30 minutes of this session is devoted to the **why** of EBM. This can be taken directly from chapters 1 & 2 of Sackett's book. The second 30 minutes is devoted to the formation of clinical questions.

Assignment for the next week: distribute Sackett's book.

- 1) Residents to read chapters 1&2 before the next lecture.
- 2) Residents to write a clinical question based upon a patient encounter during the next week.

Look at the sites for the Centre for EBM (Sackett) and the Cochrane collaboration (<http://www.cochrane.de/>), the National Guidelines Clearing House (<http://www.guideline.gov/index.asp>), the American Academy of Neurology (<http://www.aan.com/public/practiceguidelines/>), and Medline (<http://www.igm.nlm.nih.gov>).

Introduce study design types, RCCT, observational cohort, case control series, longitudinal studies (resource page: <http://cebm.jr2.ox.ac.uk/docs/studies.html>) Explain the relative merits and weaknesses of each study design. Discussion points should include the issues of causality vs. association, simple vs. complex study designs, ethical consideration, and blinding. Go over the differences and limitations between double blind, single blind and open label studies.

Assignment for the next week: 1) Read sections on diagnostic tests.

- 2) The resident must formulate a new diagnostic clinical question based upon a patient encounter in the next week.
- 3) The resident must perform a search and bring in one article to address their clinical question.
- 4) A calculator is required for the next lesson.

Week 3

Description: Statistics of EBM. There is more to EBM than sensitivity and specificity.

Have each resident present their clinical question and then review their article. What is the design of the study? Do the articles answer the clinical question? What are the limitations of the article in answering the clinical question?

Sensitivity, specificity, PPV, PPN, likelihood ratios, pre-test odds, post-test odds, and post-test probabilities. How to use these formulas to select tests for their patients. Explain the concept of a **gold standard** for diagnostic tests. Explain the importance of the likelihood ratios over the sensitivity and specificity (why a LR+ of 10 is significant, while a LR+ of 1 is not)

Explain the terms and formulas for:

- Sensitivity = $a / (a+c)$
- Specificity = $d / (b+d)$
- Pre-test probability (prevalence) = $(a+c) / (a+b+c+d)$
- Positive Predictive value (PPV) = $a / (a+b)$

Example

		Target Disorder:				
		Present	Absent			
Diagnostic test result:	Positive	80	A	20	B	100 (A+B)
	Negative	20	C	80	D	100 (C+D)
		100 (A+C)		100 (B+D)		

Sensitivity = 80 % (0.8)

This test will accurately diagnosis 80% of the subjects who have the disease (true positive).

Specificity = 80 % (0.8)

The portion of those without the disease who will be accurately diagnosed as not having the disease (true negatives)

Pre-test probability (prevalence) = 50% (.5)

The portion of the study population with the disease.

Positive Predictive value (PPV) = 80 % (0.8)

The proportion of those with an abnormal result who have the disease.

Negative Predictive value (NPV) = 80% (0.8)

The proportion of those with a normal result who do not have the disease.

Likelihood ratio positive (LR+) = 4

Ratio of true positives to false positives. An abnormal test result is four times more likely to be associated with the disease in question than not.

Likelihood ratio negative (LR-) = .25

Ratio of false negatives to true negatives. There is a one in four chance that a negative result will occur in a subject with the disease.

Pre-test odds = 1

The chance of finding an abnormal test result before the test is run. Your chances of finding the disease based upon the total population of the study group.

Post-test odds = 2

The chance of finding an abnormal test result after the test is run.

Post-test probability = 67% (2/3)

The ratio of true positives to the rest of the study population. The diagnostic test improves the ability to diagnosis the disease by 17% (from the prevalence of 50 % to 67 %)

If time permits have the residents make 2x2 tables from their articles.

Worksheet for Week 3, Resident Articles on Diagnostic Test

Complete during class on week three if time permits.

Target Disorder:

		Target Disorder:		totals
		Present	Absent	
Diagnostic test result	Positive			
	Negative			
	totals			

Sensitivity of the test:

Specificity of the test:

Pre-test probability (prevalence)

PPV

NPV

LR+

LR-

Pre-test odds = prevalence / (1-prevalence)

Post-test odds = pre-test odds x likelihood ratio

Assignment for Week 4

Calculate the items listed below based upon this fictitious synopsis:

Screening nerve conduction studies were performed on 1200 automotive workers. 650 had symptoms of carpal tunnel syndrome. Of these 523 had abnormalities on nerve conduction studies consistent with carpal tunnel syndrome. Of those without symptoms, 187 had abnormalities consistent with the diagnosis of carpal tunnel syndrome. Assuming that the symptoms of carpal tunnel syndrome are the gold standard for diagnosis, construct a 2x2 table and determine the following:

		Target Disorder:		totals
		CTS		
Diagnostic test result	Positive	Symptoms	Asymptomatic	
		Negative		

Sensitivity of the nerve conduction studies:

Specificity of the nerve conduction studies:

Pre-test probability (prevalence)

PPV

NPV

LR+

LR-

Post-test probability = post-test odds / (post test odds + 1)

Worksheet for Resident Articles for Week 4

		Target Disorder:		totals
		Present	Absent	
Diagnostic test result	Positive			
	Negative			
	totals			

Sensitivity of the nerve conduction studies:

Specificity of the nerve conduction studies:

Pre-test probability (prevalence)

PPV

NPV

LR+

LR-

Pre-test odds = prevalence / (1-prevalence)

Post-test odds = pre-test odds x likelihood ratio

Teachers Guide to the Assignment for Week 4

Calculate the items listed below based upon this fictitious synopsis:

Screening nerve conduction studies were performed on 1200 automotive workers. 650 had symptoms of carpal tunnel syndrome. Of these 523 had abnormalities on nerve conduction studies consistent with carpal tunnel syndrome. Of those without symptoms, 187 had abnormalities consistent with the diagnosis of carpal tunnel syndrome. Assuming that the symptoms of carpal tunnel syndrome are the gold standard for diagnosis, construct a 2x2 table and determine the following:

		Target Disorder:		totals
		CTS Symptoms	Asymptomatic	
Diagnostic test result	Positive	523	187	710
	Negative	127	363	490
	totals	650	550	1200

Sensitivity of the nerve conduction studies:
80.4 %

Specificity of the nerve conduction studies:
66 %

Pre-test probability (prevalence)
54.2%

PPV
73.6 %

NPV
74.1 %

LR+
2.36

Post-test probability
0.7

Week 4

Description: Analysis of therapeutic articles.

Preparation: Adequate number of copies of a therapeutic article with a high drop out rate. Tachine articles are a good source.

Go over the homework, correct their calculations.

Analysis of therapy articles brought in by the residents. Have each resident state their clinical question and summarize the article in less than 2 minutes including the study design. Review 2x2 tables.

Go over blinding and intent to treat analysis. Explain the statistics for therapy, including relative risk reduction (RRR), absolute risk reduction (ARR), number needed to treat (NNT) and 95% confidence intervals of NNT. Explain the significance of the 95 % confidence intervals.

CER (control event rate) = control events / control population

EER (experimental event rate) = experimental events / experimental population

Relative risk reduction (RR) = (CER-EER)/CER

Absolute risk reductions (ARR) = CER- EER

Number needed treat (NNT) = 1/ARR

95 % confidence interval on ARR =

$$\pm 1.96 \times \left[\frac{\text{CER} \times (1-\text{CER})}{n \text{ of controls}} + \frac{\text{EER} \times (1-\text{EER})}{n \text{ of exp. subjects}} \right]$$

95 % confidence interval on NNT = 1 / limits on the CI of the ARR

Example One: small number of subjects:

Fictitious study data of treatment of atrial fibrillation with warfarin compared to placebo.
Event = TIA or CVA

NNT = 5

95 % CI of ARR = +/- 33.95 %

The range for ARR is from 0 % to 53.95 %

The range for NNT ranges from 1.8 to infinity

Example Two: larger n

Fictitious study data of treatment of atrial fibrillation with warfarin compared to placebo. Event = TIA or CVA. The ratios are the same; the n has increased by a factor of 100

Tx		Results		totals
		Event	No Event	
	Exp. Tx	100	900	1000
	Control	300	700	1000
	Group			
	totals	400	1600	2000

RRR = 66.7 %

ARR = 20 %

NNT = 5

95 % CI of ARR = +/- 3.395 %

The range for ARR is from 16.6 % to 23.4 %

The range for NNT ranges from 4.3 to 6.

Analyze the example study with a high drop out rate. Look at how the dropouts were handled. Explain intent to treat analysis: carrying forward the last results, vs. predicting the decline in outcome measurement.

Assignment 1) Read the prognosis and economic analysis portions of Sackett's textbook.

2) Resident to develop a clinical question on prognosis for the next week.

3) Resident to search a find an article on prognosis to answer their question.

Week 5

Description: Prognosis and Economic analysis

Preparation: For prognosis bring in an article on the risk of stroke in patients with atrial fibrillation without treatment with anticoagulation. Find several articles that deal with the economic impact of diagnostic tests and treatments. Be able to discuss them in detail

- is the length of follow-up adequate for the outcome?

Assignment: The residents as a group are to perform a literature search on the clinical question:

In patients with mild closed head injury (CHI, Glasgow Coma Score \geq 13) and a non-focal neurological examination, do emergency neuroimaging studies significantly decrease the morbidity and mortality of those with surgically treatable lesions that would have been missed without emergent imaging?

Each resident must bring in a different article from their search.

Week 6

Description: class activity to develop a practice parameter.

Explain and distribute Classification of the Levels of Evidence and Recommendations based upon the levels of evidence.

Each article is reviewed and classified by two residents.

Develop 2x2 tables. Calculate relative risk (odds ratios) and the 95% confidence intervals where possible.

Review the evidence and determine if you have an answer to the question. Restate the question if necessary and develop your recommendation.

This activity can be completed in one hour if you work quickly.