Supplementary materials

Diagnosis Module

Clinical Scenario:

A 35-year-old female comes to your office complaining of epigastric pain for 4 weeks. She has been experiencing the pain immediately after meals, 6-7/10 in intensity, sometimes radiating to her chest. Very rarely associated with nausea and vomiting. She has been reducing the amount of food that she has been eating because she is very afraid that she would get the pain. She has lost 4 lbs in the last month.

She has a history of a stomach ulcer few years ago, diagnosed after the endoscopy. She had similar symptoms at that time and she was found to be H. pylori positive and was successfully treated. She has been taking Prilosec daily for the last month, with some improvement in her symptoms.

You suspect that she might have a recurrent ulcer and you would want to test her again to see if she has a re-infection with H Pylori. When you mention that she will need endoscopy done again, she becomes very anxious and starts crying, stating that she doesn't want to go thru that experience again, as she vomited for 6 hours after the previous endoscopy. You are trying to explain to her that the vomiting could have been because of anesthesia and it might not happen again, but she is very reluctant and is asking if there is any other test that she can have to diagnose this infection and she wants to have it done as soon as possible.

You know that the available serology and urease tests for H pylori are misleading, with a high percentage of false positive rates, and you know that the upper endoscopy and biopsy will provide the most accurate diagnosis. However, in light of her reluctance to proceed with the endoscopy, you remember that there is a test called STRING TEST that is non-invasive. She is asking you how good in diagnosing H. Pylori is the String Test when compared with Endoscopy?

Your search of the literature presents the following paper:

Validation of String Test for Diagnosis of Helicobacter pylori Infections
Billie Valepatino, Jacqueline Balqui, Robert H. Gilman, Alejandro Bussalleu, Willi Quino, S. Alison Finger, Livia Santivanez, Phabiola Herrara, Alejandro Piscoa, Jose Valdivia, Jaime Cok, and Douglas E. Berg
Journal of Clinical Microbiology, March 2006, p. 976-980

Diagnosis

PGY_____ PROGRAM_____

1. **Pre-test probability is best defined by which of the following statements?**
    a. The probability the patient's complaint will result in a positive testing.
    b. The probability the patient's complaint will result in negative testing.
    c. The probability the patient has the target condition based on presentation.
    d. The probability the patient does not have the target condition based on presentation.

2. **The MOST RELIABLE estimate of pre-test probability comes from which source?** a. Clinical experience
    b. Clinical Prediction Rules
    c. Clinical Research
    d. Health Surveys

3. **A positive screening test will result in which of the following actions:**
    A. Increase your testing threshold, making you less likely to order a diagnostic test
    B. Decrease your testing threshold, making you more likely to order a diagnostic test
    C. Increase your treatment threshold, making you less likely to start the treatment as you ruled out the disease
    D. Decrease your treatment threshold, making you more likely to start the treatment as you already made the diagnosis

4. **The biomarker X45 is discovered in patients with lung cancer. The serum of patients with metastatic adenocarcinoma of the lung is tested for X45. It is compared to histologic confirmation from biopsy. The pathologists were blinded to the results of the assay. The results of the study show 91% sensitivity, 87% specificity, 94% PPV, 64% NPV when compared to biopsy proven lung cancer.**
    Which of the following is FALSE regarding the validity of this test?
    a. The authors compared to an appropriate reference standard.
    b. The patients presented with a diagnostic dilemma.
    c. The physicians interpreting the test were blinded.
    d. All of the patients received the same reference standard.

5. **Researchers are attempting to simplify screening for alcoholism. Patients are asked "Do you feel guilty when you drink alcohol?" They compare this response to the CAGE questionnaire. Researchers were blinded to the answers from participants. Alcoholism is defined as answering yes to two CAGE questions. They report 99% sensitive and 94% specificity for their question. Which of the following is FALSE. regarding the validity of this test?**
    a. The authors compared to an appropriate reference standard.
    b. The patients presented with a diagnostic dilemma.

c. The physicians interpreting the test were blinded.
d. All of the patients received the same reference standard

6. **Which of the following statements best describes a positive likelihood ratio?**
   a. The likelihood that a positive test is a true positive.
   b. The likelihood that a negative test is a true negative test.
   c. The ratio between true positives and true negatives in patients with the condition.
   d. The extent in which the pre-test probability is changed based on a positive result.

7. **Which of the following best describes the degree of change from pre-test probability to post-test probability based on a likelihood ratio > 10 or < .1?**
   a. Small
   b. Moderate
   c. Large
   d. Conclusive

8. **Which of the following best describes the degree of change from pre-test probability to post-test probability based on a likelihood ratio of (1 to 2) or (.5 to 1)?** a. Small
   b. Moderate
   c. Large
   d. Conclusive

9. **You want to design a study that will evaluate the diagnostic accuracy of stress test compared with CT coronarography in 100 patients with pre-test probability in between 20-80 percent. All the patients with positive stress test will be referred to have a CT coronarography for confirmation and if the CT coronarography is positive, then they will be referred to a cardiologist. 20 patients had pre-test probability higher than 60% and 16 had positive stress tests. You decide to refer the 16 patients to a cardiologist without performing the CT coronarography to confirm the diagnosis. When you interpret the results of this study, regarding the stress test performance:**
   a. you are concerned about the validity of the results because of the potential referral bias
   b. you are concerned about the validity of the results because of the potential verification bias
   c. you are concerned about the validity of the results because of the potential observer / cardiologist bias
   d. you are concerned about the validity of the results because of the potential selection bias, as you selected the patients with higher likelihood of having a coronary syndrome based on a high pre-test probability and a positive stress test

10. **Which of the following is the appropriate way to use a likelihood ratio?**
    a. Based on the test result the likelihood of the condition is X
    b. Determine pre-test probability; apply the likelihood ratio; determine positive or negative predictive value of the test

c. Determine pre-test probability; apply the likelihood ratio; determine post-test probability
d. Determine specificity; apply likelihood ratio; determine post-test probability

Harm Module

Clinical Scenario:

Mrs. Smith is a 48-year-old female you are seeing for regular follow-up. She was in a motor vehicle accident 4 years ago and suffered pelvic and spinal fractures. She has undergone multiple operations on her pelvis, and lumbar spine to correct these. At her appointment today she states that her current pain regimen is not working well. She takes
2 tablets of hydrocodone/APAP 10/325 every 6 hours, 600 mg ibuprofen TID, pregabalin 150 mg BID, and lidocaine patches to the hip and spine. To prevent opioid induced constipation, she is taking docusate and senna. She is also taking 20 mg of paroxetine to combat depression from chronic pain. She is no longer using her walker due to pain and spends most of her time lying in bed.
Her vital signs are normal today. You perform a musculoskeletal exam that does not show any new abnormality.
You explain that she may be developing some tolerance to her hydrocodone, and her acetaminophen dose is high. You want to transition her to a sustained released medication. She is nervous about the change. During her first hospitalization she had an adverse reaction to a fentanyl patch that resulted in respiratory failure. "Can't we just increase my hydrocodone?" she asks. You ask her to consider the change and to come back in two weeks. You refill her medications and jot a little note to yourself to review the risks of starting sustained release opioids.

Your Literature Search Reveals:

Prescription Opioid Duration of Action and the Risk of Unintentional Overdose Among Patients Receiving Opioid Therapy

Matthew Miller, MD, ScD; Catherine W. Barber, MPA; Sarah Leatherman, PhD; Jennifer Fonda, BS; John A. Hermos, MD; Kelly Cho, PhD; David R. Gagnon, MD

AMA Intern Med. 2015;175(4):608-615. doi:10.1001/jamainternmed.2014.8071 Published online February 16, 2015.

Harm

PGY_____ Program_____

1. Which of the following study formats carries the lowest risk of bias when assessing harm?
   a. Case-Control Study
   b. Cohort Study
   c. Randomized Control Trial
   d. Case Series

2. Which of the following best describes a Case-Control Study?
   a. Subjects are randomized to a control group or an exposure group and observed for a target outcome.
   b. Exposed subjects and non-exposed subjects are observed for a target outcome.
   c. Subjects with a target outcome are compared to those without the target outcome and assessed for prior exposure.
   d. Subjects are exposed and observed for a target outcome.

3. When is a case control study preferred over a cohort study
   a. When the target outcome is common.
   b. When the target outcome is rare.
   c. When there are multiple target outcomes.
   d. When the target outcome occurs rapidly.

4. In determining the validity of a **Cohort** study's results, the following question(s) should be asked:
   a. Were patients similar for prognostic factors that are known to be associated with the outcome
   b. Were the circumstances and methods for detecting the outcome similar?
   c. Was the follow up sufficiently complete?
   d. All of the above

5. In determining the validity of a **Case Control** study's results, which of the following carries the **LEAST** value?
   a. The circumstances and/or indication that led to exposure similar across all subjects.
   b. The method and/or circumstance to determine exposure similar for all subjects.
   c. The degree or amount of exposure?
   d. Statistical correction of confounders was completed.

6. Which of the following best describes the impact of surveillance bias on risk factors associated with a target outcome?
   a. A false increase in the magnitude of risk.

b. A false decrease in the magnitude of risk.
c. Decreased surveillance for the risk factor.
d. Increased surveillance for the risk factor.

7. What number tells you the strength of the association between exposure and outcome in these studies?
    a. The p-value
    b. The Odds Ratio
    c. The Confidence Interval
    d. The Correlation Coefficient

8. A patient with chronic headache has recently read in a women's magazine that living in flats with raised levels of formaldehyde causes chronic headache. You perform a literature search on this topic and find several relevant studies:

    Which study design do you regard as most appropriate for this question?

    A. Prevalence study
    B. Ecological study
    C. Case control study
    D. Prospective randomized controlled study
    E. Case series

9. The following approaches were chosen in the studies you retrieved. Which one do you think is most appropriate?
    A. 100 patients with headache from a specialist headache clinic and 100 patients without headache are recruited from GP practices. The formaldehyde concentration is measured in the homes of both groups.
    B. A headache questionnaire is sent to all tenants of a housing project. At the same time a skintest for formaldehyde allergy is performed. The frequency of headache is compared between those with and without formaldehyde allergy.
    C. The formaldehyde concentration in the blood of patients with chronic headache from a pain clinic is measured twice within one year. The concentration of the first measurement is compared to the second one
    D. A headache questionnaire is given to new tenants of a housing project suspected to be contaminated with formaldehyde. The same questionnaire is administered to long-term tenants. The frequency of headache between new and long term tenants is compared.

Systematic Review Module

Clinical Scenario:

Mr. Brown is a 54-year-old male that presents to the clinic today to discuss his current medications. Since his last cardiac procedure he has suffered from easy bruising and epistaxis at least twice per month. He has a history of coronary artery disease and ischemic cardiomyopathy. His last PCI was 10 months ago with drug eluting stent (DES) placement to the mid LAD. He is currently taking aspirin 81mg, clopidogrel 75mg, atorvastatin 80mg, lisinopril 10 mg, furosemide 20 mg, and metoprolol XL 25mg. His most recent ejection fraction is 40%. He is NYHA class II heart failure.

Vitals: BP – 115/75 P-72 BMI – 32
His exam is positive for dried blood inside the nares bilaterally. His skin exam reveals small bruises on his forearms and left anterior leg. His cardiovascular and pulmonary exams are without significant abnormality.

At an appointment with his cardiologist one month prior he asked about stopping clopidogrel. The cardiologist would prefer to keep him on clopidogrel for the rest of his life. He asked, "What would you rather have, a nose bleed or a heart attack?" Mr. Brown asks for your opinion on the matter. You inform him that you will need some time to review the literature. You ask him to return in one week to discuss this further.

Your search of the literature presents the following paper:

Longer- Versus Shorter-Duration Dual-Antiplatelet Therapy After Drug-Eluting Stent Placement A Systematic Review and Meta-analysis

Frederick A. Spencer, MD; Manya Prasad, MBBS; Per O. Vandvik, MD, PhD; Devin Chetan, HBA; Qi Zhou, PhD; and Gordon Guyatt, MD

Annals of Internal Medicine • Vol. 163 No. 2 • 21 July 2015

Systematic Review

PGY Year_____ Program_____

1. When comparing Narrative Reviews versus Systematic Reviews, it is important to know that Systematic Reviews will:
    a. Often address more than one clinical question
    b. NOT include a comprehensive search for primary articles
    c. HAVE explicit inclusion and exclusion criteria for primary studies
    d. Do NOT evaluate quality of articles

2. A Meta-Analysis:
    a. Should always be based on a systematic review
    b. Should always be included in a systematic review
    c. Employs statistical methods to combine data from primary studies d. A + B
    e. A + C
    f. All of the above

3. In order to be considered valid, a systematic review must ask a sensible question. To formulate a sensible question the authors must consider which of the following:
    a. The Range of Patients
    b. The Range of Treatments
    c. The Range of Outcomes
    d. The similarity of the Results
    e. A-C
    f. All of the Above

4. To be valid, a systematic review should also include an exhaustive and detailed search for relevant studies. This often includes searching:
    a. Database searches and Registry of Controlled Trials
    b. Recently published abstracts from scientific meetings
    c. Unpublished data (gray literature)
    d. Pharmaceutical companies
    e. A + B
    f. All of the above

5. It is important for the authors of a systematic review to explain their search strategy in order to:
    a. Ensure that there is no conflict of interest.

b. Decrease publication bias.
c. Increase the likelihood of their study being published.
d. Ensure that it is reproducible.

6. The validity of a systematic review is dependent upon all of the following except:
    a. An assessment the quality of the original studies
    b. Inclusion of available unpublished data
    c. The sensitivity analysis.
    d. Evidence that the assessments can be reproduced

7. Funnel Plots attempt to:
    a. Summarize results in an easy to understand visual
    b. Identify Reporting Bias
    c. Identify quality among studies
    d. Summarize the methods used to search for primary studies

8. Variability (I^2) Describes the percentage of the variability in effect estimates that is due to underlying differences. What is the highest acceptable level of variability?
    a. a value of < 10% represent acceptable variability.
    b. a value of < 20% represent acceptable variability.
    c. a value of > 50% represent acceptable variability.
    d. a value of > 80% represent acceptable variability.

9. A Forest Plot can be used in a Meta-Analysis:
    a. To understand the results of each study
    b. To understand the cumulative effect
    c. To understand variability among studies
    d. To understand the bias
    e. A-C
    f. All of the above

10. If a meta-analysis is considered to have low variability between studies, the confidence intervals should…
    a. All overlap
    b. Should never overlap
    c. Should all be on the same side as one
    d. Should be narrow

Therapy Module

Clinical Scenario:

Mr. Jones is a 53-year-old male that presents to your office for hospital follow-up after a myocardial infarction. The patient presented to the hospital with acute chest pain. He was diagnosed with an NSTEMI. He underwent urgent percutaneous coronary intervention (PCI). A drug-eluting stent was placed in the patient's circumflex artery. His heart function was normal after PCI and his ECG improved. He took no medication prior to hospitalization. His hospital course was uncomplicated and he was discharged 24 hours after his procedure. His medications are aspirin 81mg, ticagrelor 90 mg BID, atorvastatin 80mg, metoprolol XL 50mg, lisinopril 5mg, SL nitroglycerin .4mg PRN, and amlodipine 5 mg.

Today, Mr. Jones is doing well. He denies any angina, shortness of breath, and lower extremity edema. He complains of some fatigue. His cardiologist told him that the fatigue is expected and should improve. He has not attempted to exert himself. His vital signs are as follows: BP 125/80, P-72, RR – 12, afebrile, BMI 28. His cardiovascular exam is without abnormality today. You review his lab work from the hospital stay. His CBC and CMP were within normal limits, BNP was 51, Hgb A1c was 5.5, TSH was 1.4, Total Cholesterol was 215, TG's were 150, LDL was 134, and HDL was 32.

You inform Mr. Jones that he is doing very well after this very serious event and he is on appropriate therapy. You can tell that he is very anxious and unsatisfied with your assessment. He wants to know if there is anything else he can take to prevent another heart attack. He says "I feel like my heart is gonna stop. You have to help me." You validate his concerns. You reiterate that he is on very good medication that will keep his heart healthy. You tell him that you will do some studying to see if there are any other interventions that will prevent a heart attack. You ask him to follow-up in two weeks.

You type Mr. Jones question as a reminder in your smart phone. When you get home that night you do a quick literature search and find a recent publication in
NEJM that may help Mr. Jones. You get out your appraisal sheet and go to work.

Ezetimibe Added to Statin Therapy after Acute Coronary Syndromes

Cannon, Christopher P., Michael A. Blazing, Robert P. Giugliano, Amy McCagg, Jennifer A. White, Pierre Theroux, Harald Darius, et al.

New England Journal of Medicine 372, no. 25 (June 18, 2015): 2387–97. doi:10.1056/NEJMoa1410489.

Therapy

PGY Year _____ Program_____

1. Rank these from strongest level of evidence (1) to least (4).

A. Randomized controlled trial
B. Meta-analysis of randomized controlled trial
C. Qualitative research
D. Narrative review

2. In determining the validity of a therapy study's results, the following question(s) should be asked:

A. Were the patients randomized?
B. Was randomization concealed?
C. Was intent to treat analysis performed?
D. Were patients in the control and experimental group the same?
E. All of the above

3. The concealment of randomization in a RCT refers to:

A. The patients are not aware in which group they are getting assigned
B. The investigators are not aware about the intervention in each group
C. The patients and the investigators are not aware of the intervention for each group
D. The patients and the investigators are not aware of the process of assigning the patients to different groups
E. None of the above

4. What is intent to treat analysis?

A. All patients are treated the same within their own group (experimental and control).
B. Patients are analyzed in the group that they were randomized.
C. Patients with bad outcomes will be treated within standard therapy.
D. Based on the study results, the investigators will recommend treatment impartially with the more efficacious agent (experimental agent or control agent). E. None of the above.

5. The precision of the estimate of the treatment effect refers to:

A. How significant is the Relative Risk?
B. How significant is the Absolute Risk when compared with the Relative Risk?
C. Depends of the width of the Confidence Intervals

D. Depends on the sample size of the trial
E. None of the above

Use the following scenario for #6-8: Researchers studied a new drug that they claim "significantly improves mortality" for acute ischemic stroke patients compared to the current standard therapy. You fervently review their results and find that this randomized controlled trial studied 1000 patients (500 in each of two arms). The experimental group had a mortality rate of 1% vs 2% in the control (standard therapy group).

6. What are the relative risk (RR) and relative risk reduction (RRR) in this trial?

A. RR - 1%, RRR - 2%
B. RR - 2%, RRR - 1%
C. RR - 50%, RRR - 50%
D. RR - 100%, RRR - 0%
E. RR - 0%, RRR - 100%

7. What are the absolute risk reduction (ARR) and number needed to treat (NNT) for this trial?

A. ARR - 100%, NNT - 1
B. ARR - 50%, NNT - 2
C. ARR - 200%, NNT - 50 D. ARR - 1%, NNT - 100
E. None of the above.

8. True (A) or False (B): In reporting clinical data, using the ARR and NNT, can inflate the magnitude of study results.