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Patients and Populations
Medical Decision-Making
Shifting Probabilities and Questions

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Learning Objectives for Today

- By the end of this lecture, you will…
  - describe Bayesian probabilistic rules, as they apply to a basic diagnostic question
  - summarize how uncertainty in diagnostic reasoning interacts with trust of the practitioner.
  - explain the difference between background and foreground clinical questions
  - recognize how individual targeted searches for the answers to clinical questions drive self-directed learning that is crucial for all practitioners
  - be able to craft foreground questions for both diagnosis and treatment, using the PICO format

A Clinical Tale

- 20 year-old woman presents for genetic testing
- Mother had breast and ovarian cancer, likely has the BRCA gene (autosomal dominant)
- With this assumption, the patient's likelihood of having the gene is…50%
- She decides not to get tested.

The Tale Continues…FFwd

- At age 75 she has not been diagnosed with breast or ovarian cancer.
- Is her probability of having the BRCA gene different at age 75 than it was at age 20?
  - Yes: it is lower
  - How much lower?

Conditional Probabilities

- What is the probability of event B, given an event A? Written as P(B | A).
  - Example: P (BRCA | no breast cancer)
- Key concept:
  - Conditional probabilities can be combined with prior probabilities to create joint probabilities

Basic Probabilistic Rules
Examples of types of Events

- Dependent events: occurrence of 1 depends to some extent on the other
  - Example: The same person passing step 1 of the boards and then passing step 2 of the boards 2 years later.
- Independent events: both can occur
  - Example: 2 different people passing step 1 of the boards (abiding by the honor code)
- Mutually exclusive events: cannot both occur
  - Example: A person getting >250 on step 1 of the boards, or the same person getting 220-250 on step 1.

Combining Probabilities of Events

- Pr (A $\cup$ B) = Pr (A) + Pr (B)
  - If A and B are mutually exclusive events
- Pr (A $\cap$ B) = Pr (A) * Pr (B)
  - If A and B are independent events
- Pr (A $\cap$ B) = Pr (A) * Pr (B|A)
  - If A and B are dependent events (Joint probability)

$\cup$ = OR $\cap$ = AND

Back to our story

75 yo woman whose mother very likely had the BRCA gene, but who has not herself been diagnosed with breast cancer.

- Our patient wants to know:
  - What is P (BRCA | no breast ca)?

Considering both sides…
Dependent Events

$$Pr(A \cap B) = Pr(A) * Pr(B|A)$$

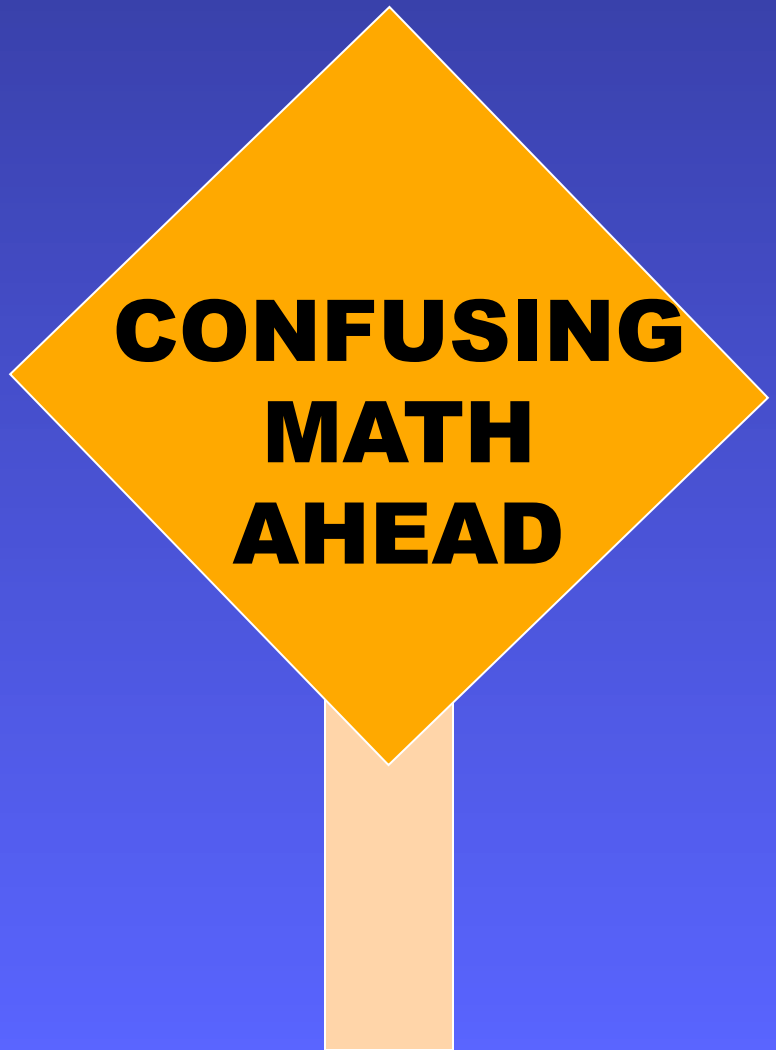
- Step 1:
  P (BRCA and no breast cancer)
  = P(BRCA) * P(no breast ca | BRCA)
  = 0.5 * 0.3 (from studies)
  = 0.15

- Step 2:
  P (NO BRCA and no breast ca)
  = P(NO BRCA)*P(no breast ca|NO BRCA)
  = 0.5 * 0.875(from studies)
  = 0.4375

But that doesn't tell the full story…

- Joint probabilities
  - P (BRCA and no breast ca) = 0.15
  - P (NO BRCA and no breast ca) = 0.4375
- The assumption is that these are NOT independent events.
- Again, our patient wants to know:
  - What is P (BRCA | no breast ca)?

WARNING



Step 3: Bayes Theorem

- Conditional probability is the relative proportion of the relevant joint probability to the sum of all the joint probabilities.

- P(BRCA | no breast ca)

$$= \frac{P(\text{BRCA \& no breast ca})}{P(\text{no breast ca})}$$

$$= \frac{P(\text{BRCA}) * P(\text{no breast ca} \mid \text{BRCA})}{P(\text{no breast ca})}$$

- P (no breast ca) = sum of all the joint probabilities
  - P (no breast ca & BRCA)
  - P (no breast ca & NOT BRCA)

Applying Bayes Theorem

- P (BRCA | no breast ca) =

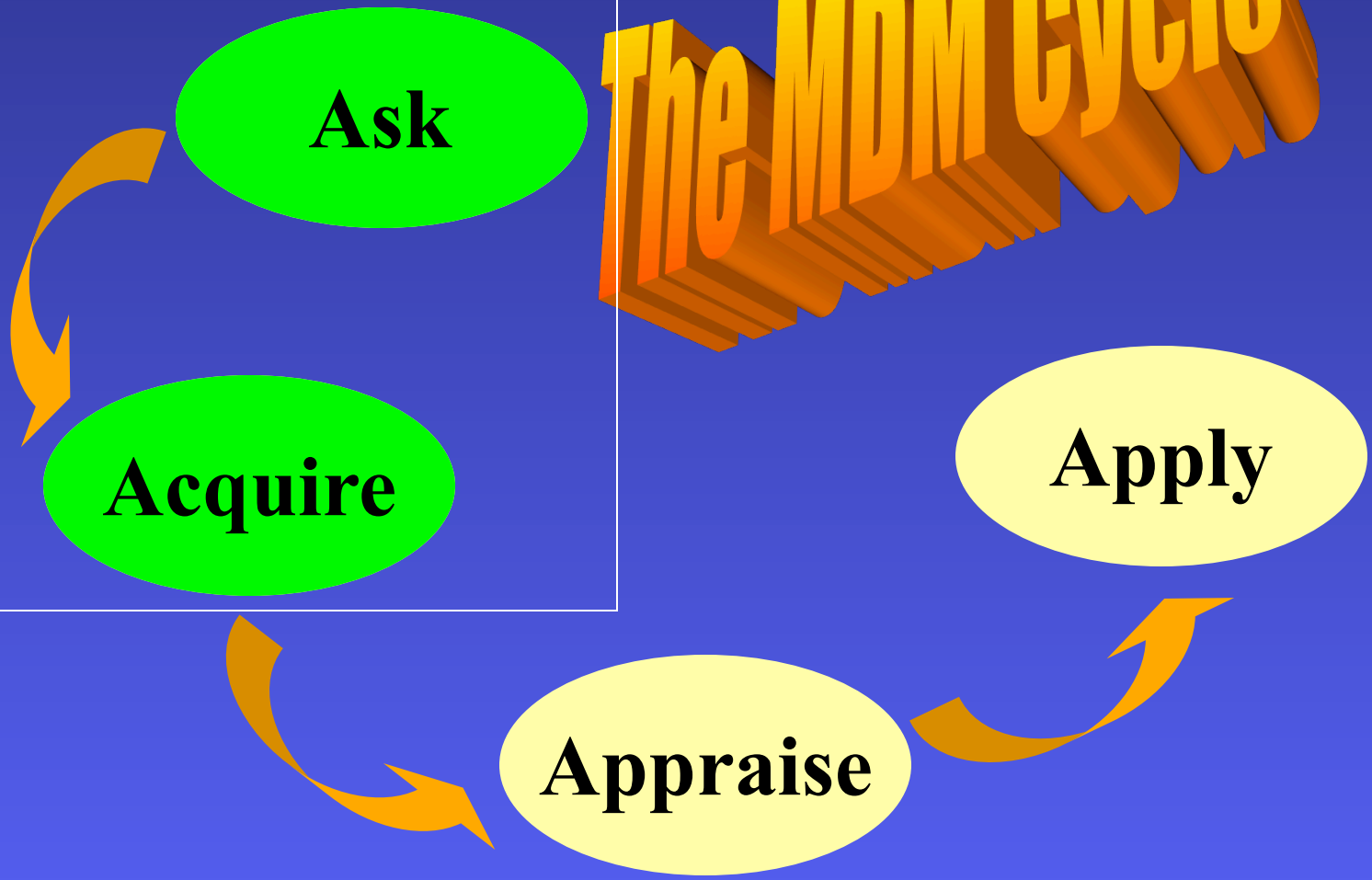
$$\frac{0.15}{0.15 + 0.4375} = 26\%$$

- 26% is significantly lower than 50% (our prior probability)

Why is this important?

- Illustration of changing probabilities, and shifting uncertainty…
  - …because of test results
  - …because of events
  - …because of time
- Fundamentally, clinicians deal with shifting probabilities and uncertainty with each patient they encounter
  - Many tools to help (Bayes, 2x2, Likelihood ratios)

Thread 1: Information Retrieval



Who is this man?

Frank Gorshin - a.k.a. “The Riddler”

Riddle me this...

- How many questions do clinicians ask while they care for patients?

4 per patient

- Why is question-generation a critical skill?

(1) Targeting Information Resources
(2) Generating Search Terms

Patient Care: Questions → Decisions

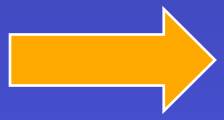
- Step 1: Question → Search for Answer
- Step 2: Assess the strength of answer
- Step 3: Weigh against:
  - Patient Values
  - Physician Values
  - Society's Values

The Well-Structured Clinical Question

- Purposes
  - Target resources
  - Define search terms
  - Define what you and the patient care about
- Two Types
  - Background
  - Foreground

Anatomy of a Background Question

- What
- How
- Where
- When
- Who
- Why



- Disorder
- Syndrome
- Finding
- Health state
- Concern

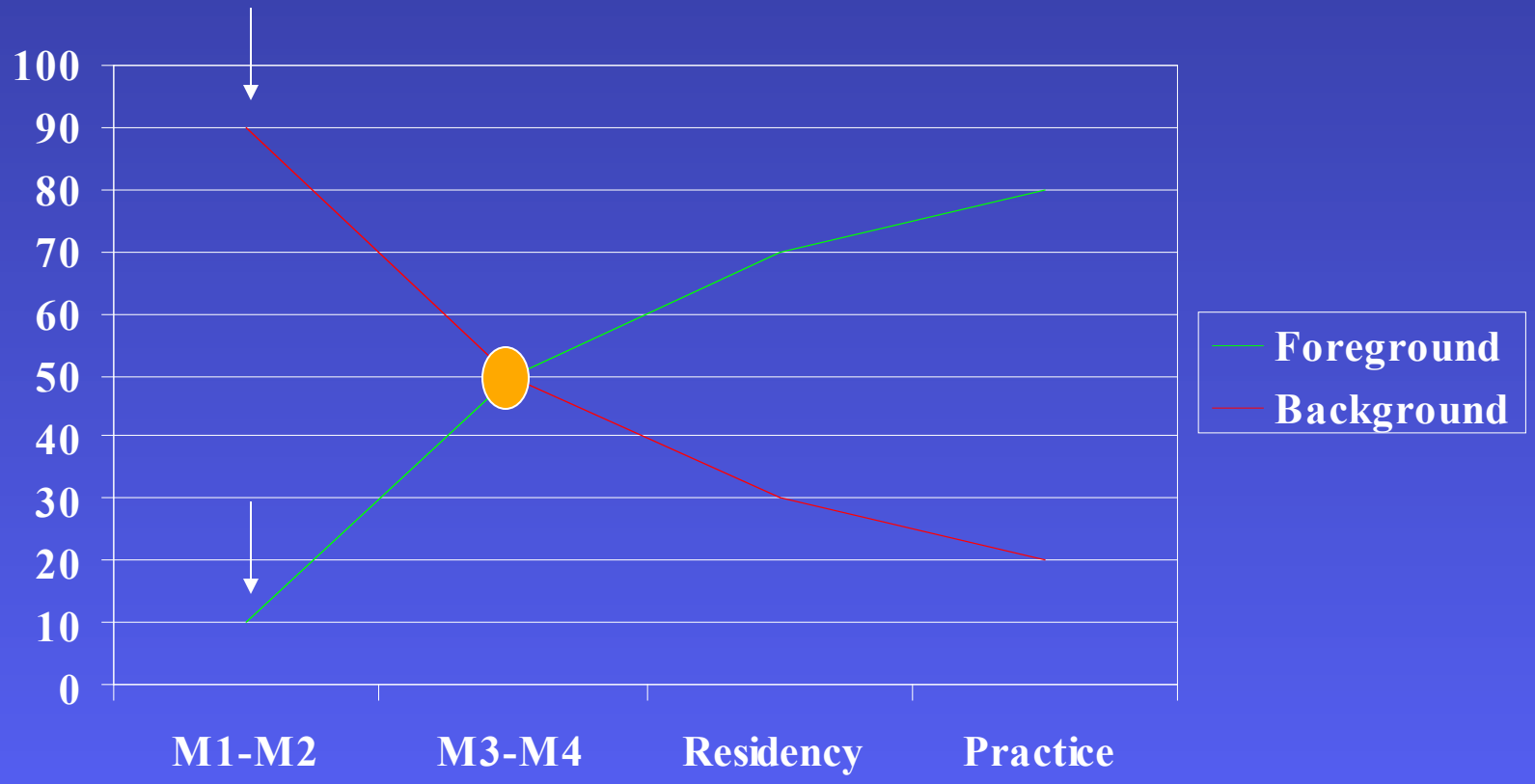
Background Questions -- Examples

- Who should get influenza vaccine and when?
- Which drugs to treat HIV can cause pancreatitis?
- What is the metabolic pathway for cholesterol synthesis?
- Why do patients with sleep apnea have high blood pressure?

Background vs. Foreground Questions

- Background: Designed to improve general knowledge about a subject
- Foreground: Patient-specific questions, strong implications for decisions, often with comparisons

An Evolution in Question Type



Background Questions: A Case

Using the following case, jot down 2 **questions** with your partner that may help you care for this patient:

A 42 year old woman comes to her primary care practitioner's office for follow up of her diabetes. She is currently on glyburide 10 mg twice daily. However, her morning and evening blood sugars still stay elevated. You are the medical student who sees this patient with your attending. Afterwards, your attending asks whether you think she should add metformin to her regimen. You say that you don't know because your knowledge of diabetes medications are sketchy.

Background Questions

- What kind of medication is glyburide?
- In what classes of medication do metformin and glyburide fall?
- What is the initial dosage of metformin?
- What are the adverse effects of metformin that I must be cautious about?
- Is it safe to be on glyburide and metformin at the same time?

Sources for Background Questions

- Course notes, lectures, syllabi
- Textbooks
  - MD Consult
  - Stat!Ref
  - DynaMed
- Review articles
- Practice Guidelines

Foreground Questions -- Examples

- In patients with chronic atrial fibrillation over the age of 70, does warfarin anticoagulation reduce the rate of stroke and death when compared with aspirin?

Therapy

- In patients with acute chest pain of less than 6 hours' duration, what is the diagnostic accuracy of a single troponin level when compared with serial EKG's and enzymes?

Diagnosis

Foreground Questions -- Examples

Therapy

- In patients with chronic atrial fibrillation over the age of 70, does warfarin anticoagulation reduce the rate of stroke and death when compared with aspirin?

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PICO: A Tool to Structure the Foreground Question

	Therapy	Diagnosis
P	Patient Pop	Disease
I	Intervention	Test
C	Comparison	Gold Standard
O	Outcome	Accuracy

he MDM Cycle

Apply

Appraise