

BAYES, MEDICAL DIAGNOSTICS, AND NOMOGRAMS

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Acknowledgements

This talk is based on:

Doc, What Are My Chances?

The UMAP Journal 32 (4): 279 – 298 (2011)

Joe Marasco, Ron Doerfler and Leif Roschier



(Pebble Beach)



(Chicago)



(Helsinki)

For more information, see:

comap.com (UMAP Journal publisher)

modernnomograms.com (nomograms)



Medicine Today

- ▣ Intensive use of high-tech
 - Diagnostic imaging
 - Surgical advances(e.g. laparoscopy)
 - Robotics (e.g. daVinci)
 - Genome sequencing
 - Pharmaceuticals
- ▣ Science and mathematics lagging
 - Evidence-based medicine (1990)
 - Education of clinicians
 - Patient empowerment



Road Map of the Talk

Medical Diagnostics



Bayes' Theorem

Nomography



Road Map of the Talk

Medical Diagnostics

It's All About Probabilities



Bayes' Theorem

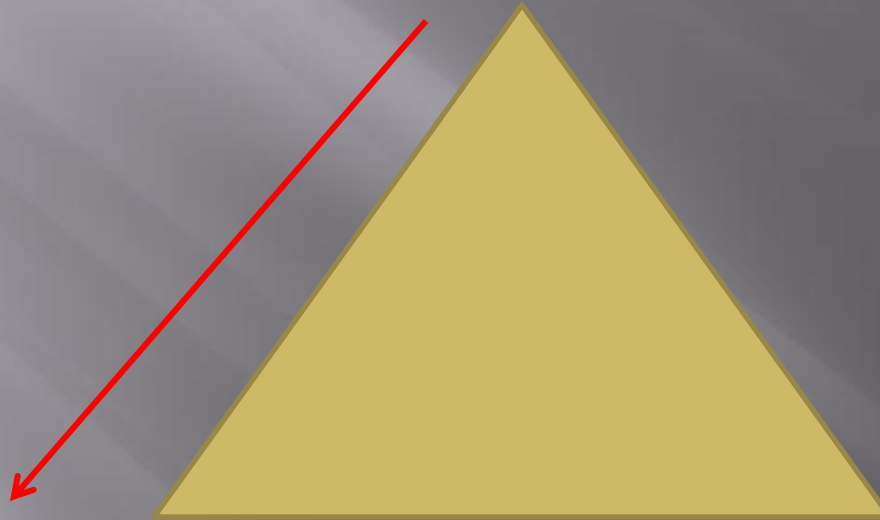
Nomography



Road Map of the Talk

Medical Diagnostics

It's All About Probabilities



Bayes' Theorem

Math for Updating Probabilities
Based on Test Results

$$P_{\text{OLD}} + \text{Test} = P_{\text{NEW}}$$

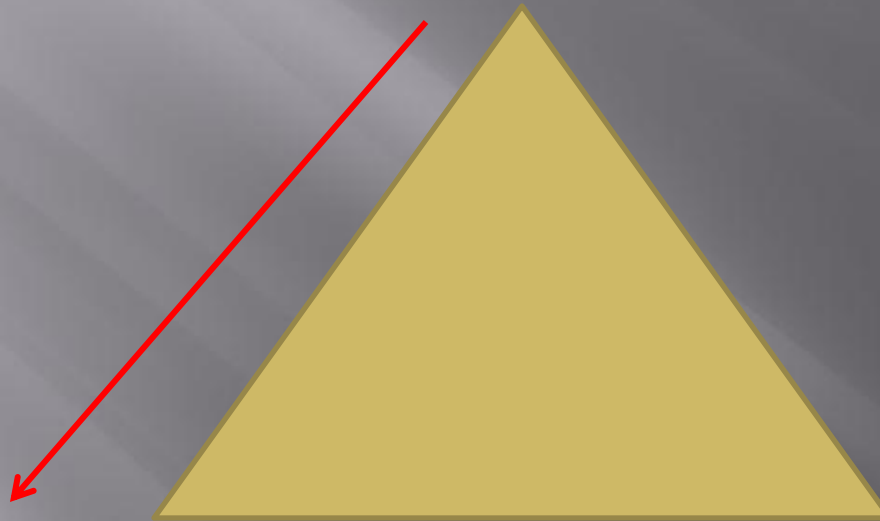
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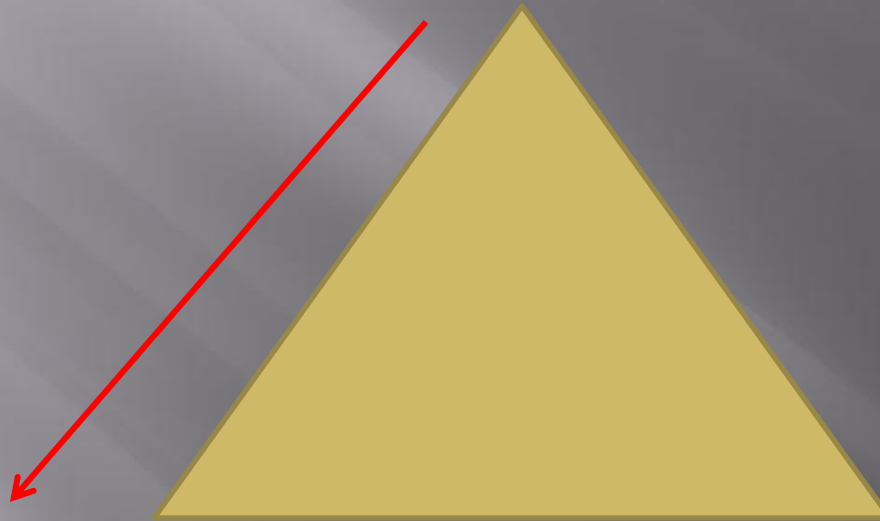
Graphical Technique for
Doing the Math



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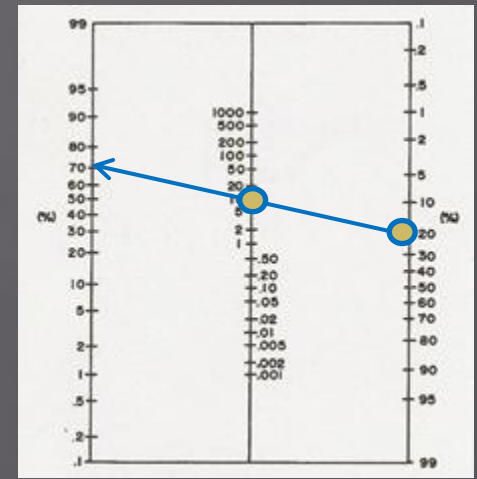
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Bayes' Theorem

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P_{NEW} Test P_{OLD}

Nomography

Graphical Technique for
Doing the Math



Example: PSA Screening



Source: Health Dialog. 2010. The PSA test – What you need to know. Video, 1:24 min.
http://www.youtube.com/watch?v=ZJS_jskR39k . Uploaded 25 February 2010.



“So, the test isn’t perfect.”

Men over 50	Healthy	Diseased	Total
PSA $\leq$ 4	77	15	92
PSA $>$ 4	5	3	8
Total	82	18	100

- ▣ We agree
 - Screening misses 83% with prostate cancer
 - 15 false negatives out of 18 total
 - $>$ 50% negative biopsy rate
 - 5 false alarms out of 8 positives
- ▣ Wrong cutoff?
 - PSA = 4 is best trade-off
- ▣ 80% “overall accuracy” misleading
- ▣ Test characterization problem



Back to Square One

- ▣ Test characterization depends on usage
- ▣ Test only one part of diagnostic protocol
- ▣ Reasonable diagnostic protocol
 - Keeps physician in the loop
 - Employs scientific method
 - Uses historical data
 - Simple
 - Easy to explain
- ▣ Candidate: Bayes' Theorem





Bayes in a Nutshell



The Scientific Method

1. Initial probability theory is valid
2. Do experiment
3. Result either tends to confirm or refute theory
4. Update: New probability theory is valid depends on initial probability, experimental result and *strength* of experiment
5. New probability becomes the initial probability for next cycle
6. Go to 1 (iterative approach)

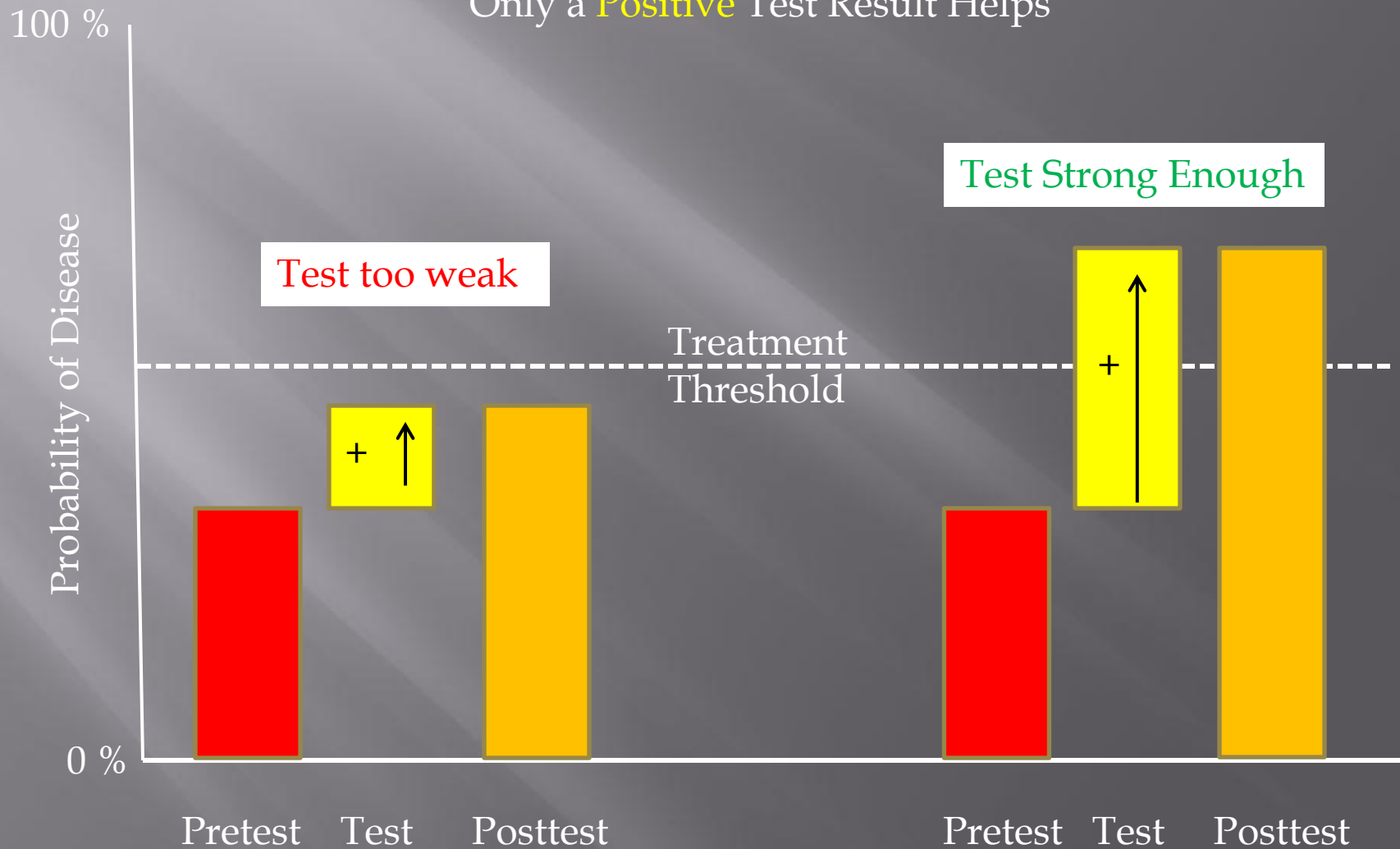
Diagnostic Protocol

1. Doctor's estimate of probability of disease based on history, symptoms, examination, etc.
2. Perform diagnostic test
3. Test comes back positive or negative
4. Update: New estimate of probability of disease based on prior estimate, test result and *test strength*
5. New estimate is starting point for next test, if necessary
6. Go to 2, if necessary



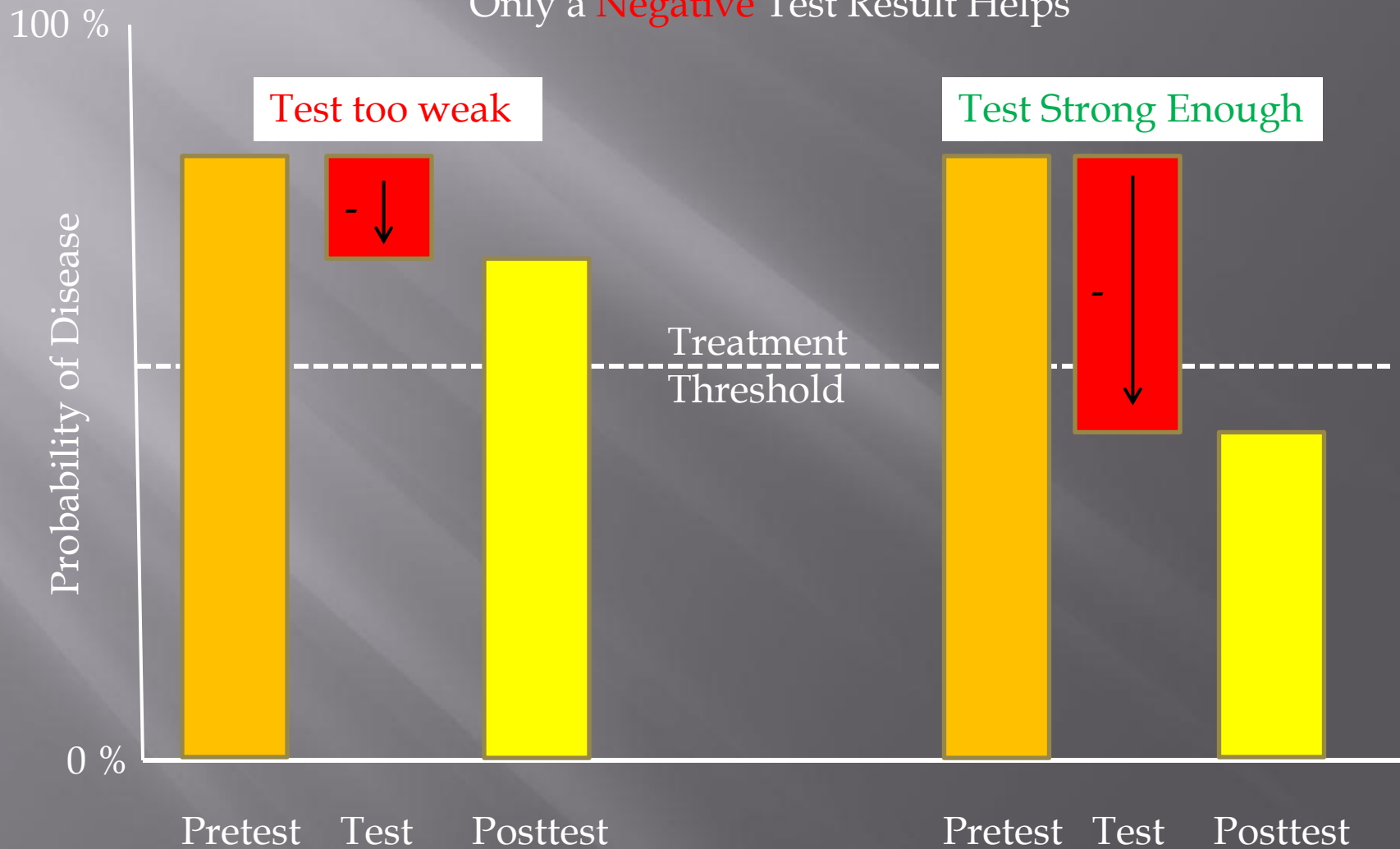
Pretest Probability Below TT

Only a **Positive** Test Result Helps



Pretest Probability Above TT

Only a **Negative** Test Result Helps



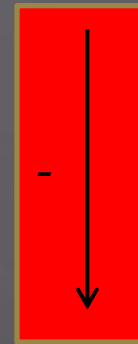
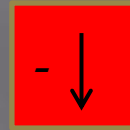
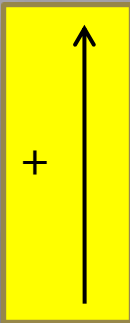
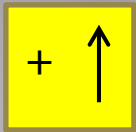
Bayes: Pre x LR = Post

Test too weak

Test Strong Enough

Test too weak

Test Strong Enough



Positive Test Result

Negative Test Result

LR+

- Length of “up arrow”
- Odds multiplier
- Always greater than or equal to 1

LR-

- Length of “down arrow”
- Odds multiplier
- Always less than or equal to 1

These two numbers, called Likelihood Ratios (LR), completely characterize the test.

Algebra: The Unanticipated Toe-Stubber



- ▣ Waltzing with Bayes
 1. Pretest Probability → (algebra) → Pretest Odds
 2. Apply Bayes: Posttest Odds = Pretest Odds × LR
 3. Posttest Odds → (algebra) → Posttest Probability
- ▣ Many tests specified by sensitivity and specificity
 - (Sensitivity , Specificity) → (algebra) → (LR+ , LR-)
- ▣ Nomograms eliminate mechanical problem



Nomography in a Nutshell



- ▣ Developed in 1890's by Maurice d'Ocagne
- ▣ Bespoke paper Slide Rule (w/o slide)
- ▣ Algebraic relationships rendered geometrically
- ▣ Provides insight through visualization
- ▣ Draw straight line from one scale to another; answer is found where line intersects 3rd scale
- ▣ 75-year run in engineering and medicine
- ▣ Went out of fashion with advent of pocket calculators and computers (circa 1970's)
- ▣ Very easy to use, can be very difficult to craft



CORRESPONDENCE

Letters to the Editor are welcome and will be published, if found suitable, as space permits. Like other material submitted for publication, they must be typewritten *double spaced* (including references), submitted in duplicate, must not exceed 1½ pages in length and will be subject to editing and possible abridgment.

NOMOGRAM FOR BAYES'S THEOREM

To the Editor: The interest in Dr. Katz's probability graph (N Engl J Med 291:1115, 1974) causes me to offer a solution to the Bayes's rule in the form of a nomogram (Fig. 1). $P(D)$ is the probability that the patient has the disease before the test.

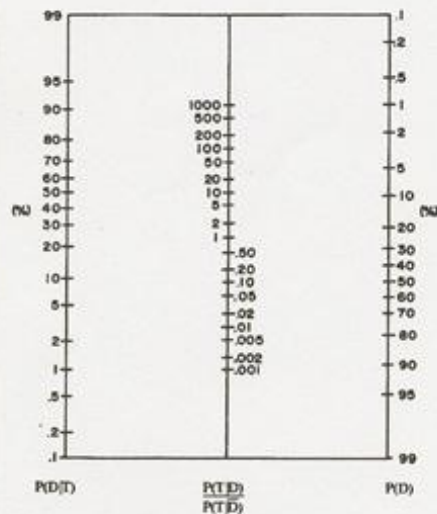


Figure 1. Nomogram for Bayes's Theorem.

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$P(D|T)$ is the probability that the patient has the disease after the test result. $P(T|D)$ is the probability of the test result if the patient has the disease, and $P(T|\bar{D})$ is the probability of the test result if the patient does not have the disease. With this terminology the usefulness of both positive and negative test results can be assessed. A line drawn from $P(D)$ on the right of Figure 1 through the ratio of $P(T|D)$ to $P(T|\bar{D})$ in the center of Figure 1 gives $P(D|T)$ on the left of Figure 1.

With Dr. Katz's renovascular hypertension example: $P(D) = 10\%$, $P(\text{Positive IVP}|D) = 100\%$, and $P(\text{Positive IVP}|\bar{D}) = 10\%$. The ratio of $P(\text{Positive IVP}|D)$ to $P(\text{Positive IVP}|\bar{D})$ is 10. A line drawn from $P(D) = 10\%$ through the ratio of 10 gives $P(D|\text{Positive IVP}) = 53\%$.

The above approach can also be used to examine the usefulness of a negative test result. The ratio of $P(\text{negative test}|\bar{D})$ to $P(\text{negative test}|D)$ is calculated and marked on the center line of Figure 1. A line drawn from $P(D)$ through this new ratio gives $P(D|\text{negative test})$ on the left of Figure 1.

TERRENCE J. FAGAN, M.D.
Baylor College of Medicine

Houston, TX

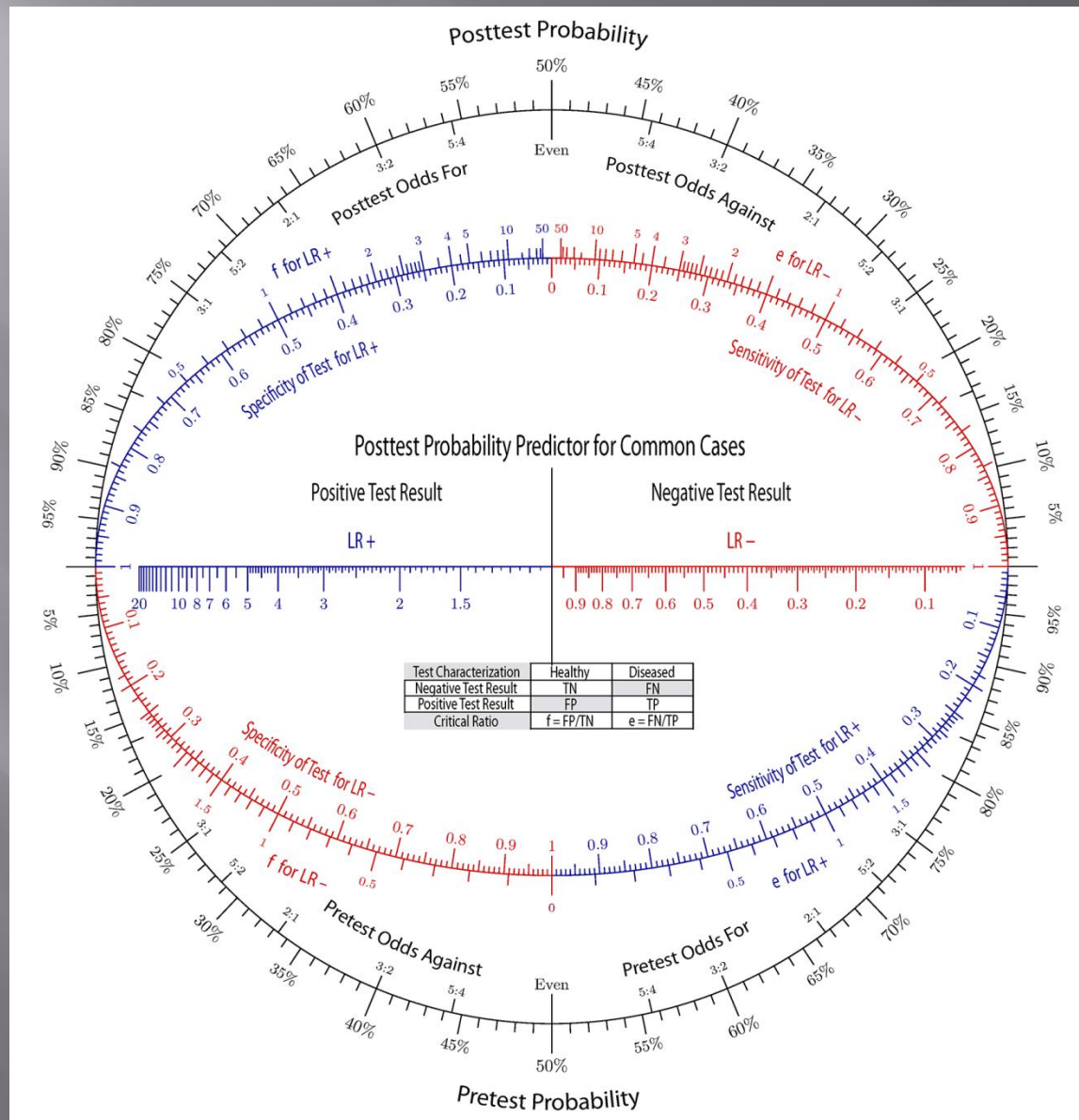
Enter Dr. Fagan

- ❑ Arrives end of nomographic era
- ❑ Letter to NEJM, July 1975
- ❑ Elegant
- ❑ Minimalist
- ❑ Became “Fagan Nomogram”
- ❑ Cited hundreds of times over the following 35 years
- ❑ Not widely used
- ❑ Not improved upon
- ❑ Until 2011

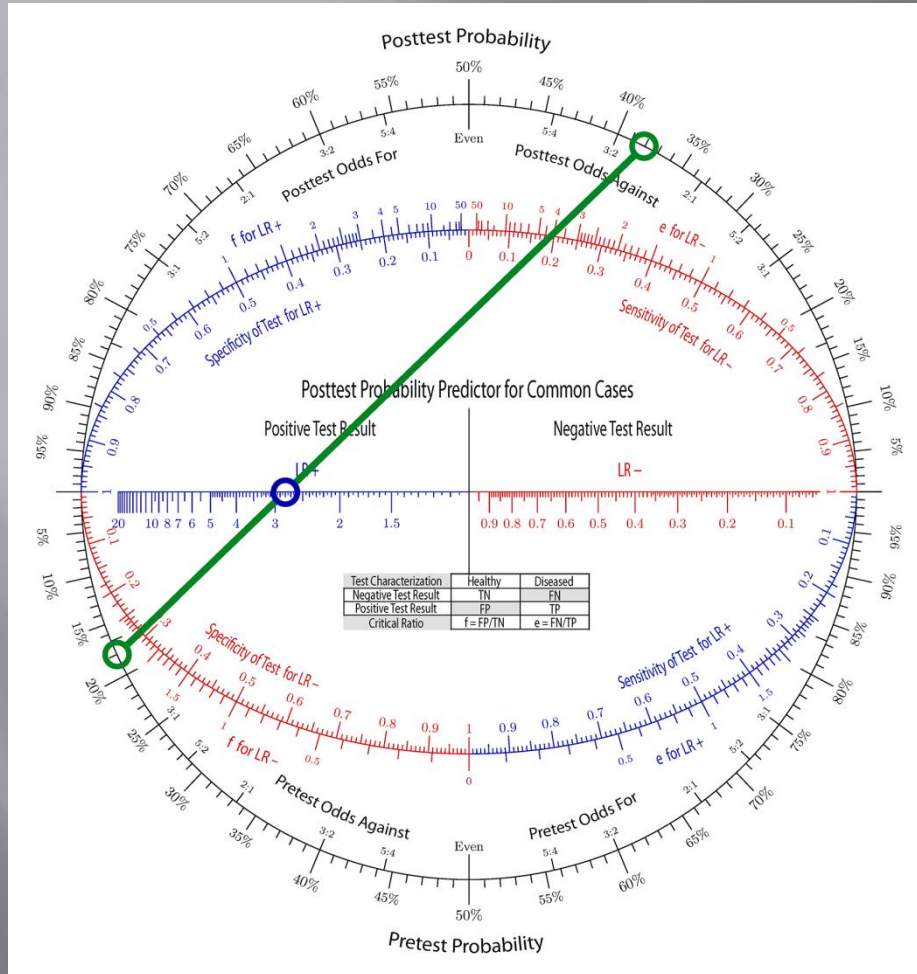
← Please respect NEJM's copyright



A New Bayes' Nomogram



PSA Screening Revisited



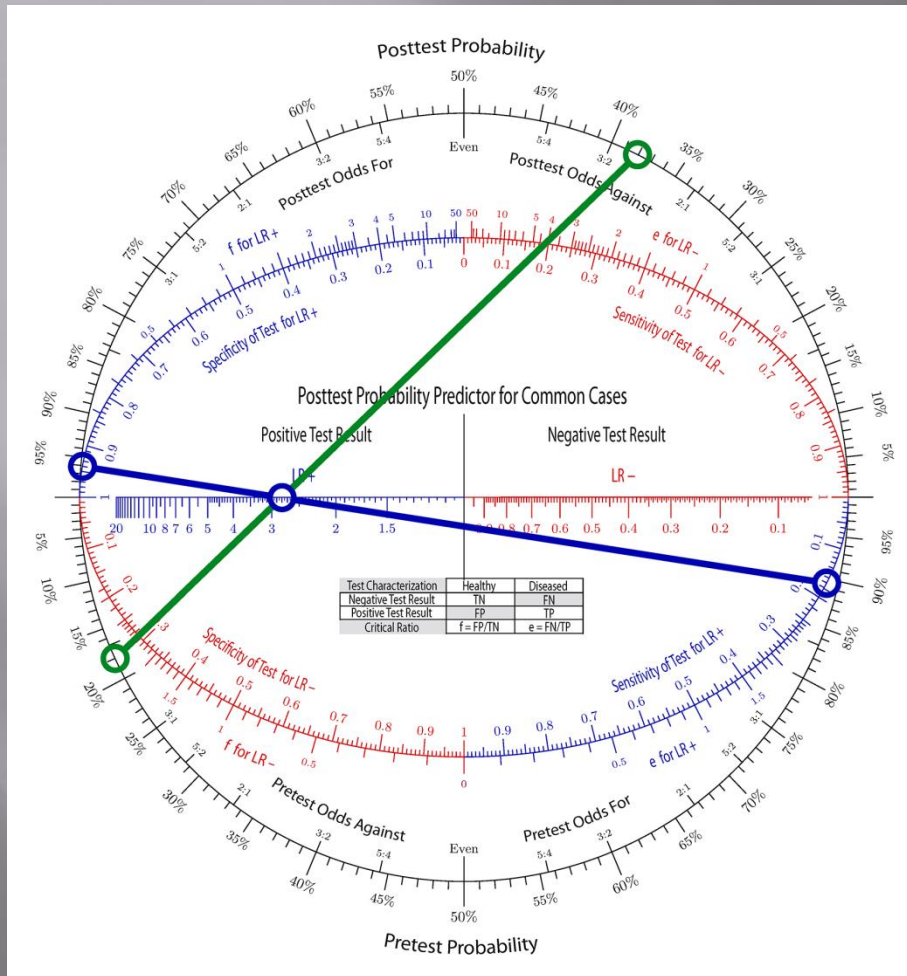
Men over 50	Healthy	Diseased	Total
PSA ≤ 4	77	15	92
PSA > 4	5	3	8
Total	82	18	100

1. This test has an $LR+ = 2.8$
2. Absent any other info, Pretest Probability = 18%
3. Assume test comes back positive
4. Find 18% on Pretest Probability on scale at bottom
5. Find 2.8 on $LR+$ scale in middle
6. Determine Posttest Probability of 38% on scale at top

Conclusion: If treatment threshold is 50%, this test is not useful for routine screening



When LR+ is Unknown



1. This test has
 - Sensitivity = 0.17
 - Specificity = 0.94
2. Locate 0.17 on lower right ellipse (blue)
3. Locate 0.94 on upper left ellipse (blue)
4. Connect these two points
5. LR+ value is now determined: 2.8
6. Proceed as before

Conclusion: If treatment threshold is 50%, this test is not useful for routine screening

Mopping Up

- ▣ Similar analysis for LR-
- ▣ Nomogram has other scales to determine all parameters from the 2x2 matrix
- ▣ In practice, sensitivity and specificity are the most commonly listed parameters
- ▣ Test parameters are cohort-dependent and evolve over time as more data are obtained
- ▣ Thus protocol is doubly-Bayesian
 - Individual's posttest probability is a Bayesian update based on test parameters
 - Over time, new data cause a Bayesian update on the test parameters themselves
- ▣ There is a second new nomogram for rare diseases (very low pretest probabilities requiring high LR+)



The New Nomography

- ▣ Problem: Construction of good nomograms is non-trivial
- ▣ Solution: PyNomo
 - Python package for creating nomograms
 - Input: Python script describing all aspects of the relationships and the display
 - Output: Camera-ready PDF or EPS
 - Vector graphic precision
 - Written by Leif Roschier
 - Open source
 - Get information at pynomo.org
- ▣ All our nomograms were created using PyNomo
- ▣ Ask me about iPad support



THANK YOU

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pynomo.org

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