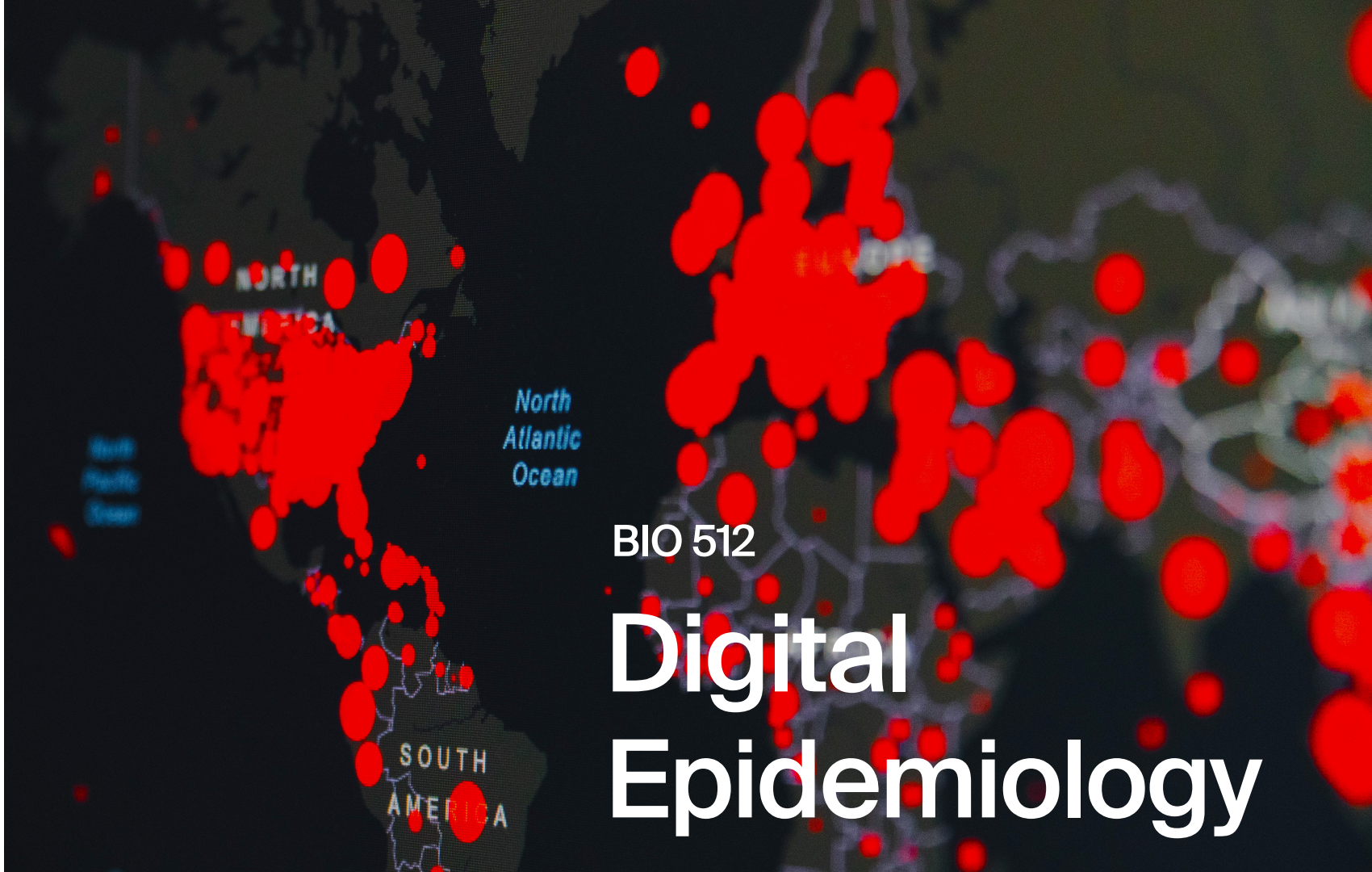


BIO 512

Digital Epidemiology

Testing & Diagnostics
Learning Objectives

- Quantitative framework for testing accuracy
- Sensitivity & specificity
- ROC
- Positive / negative predictive values
- Likelihood ratios

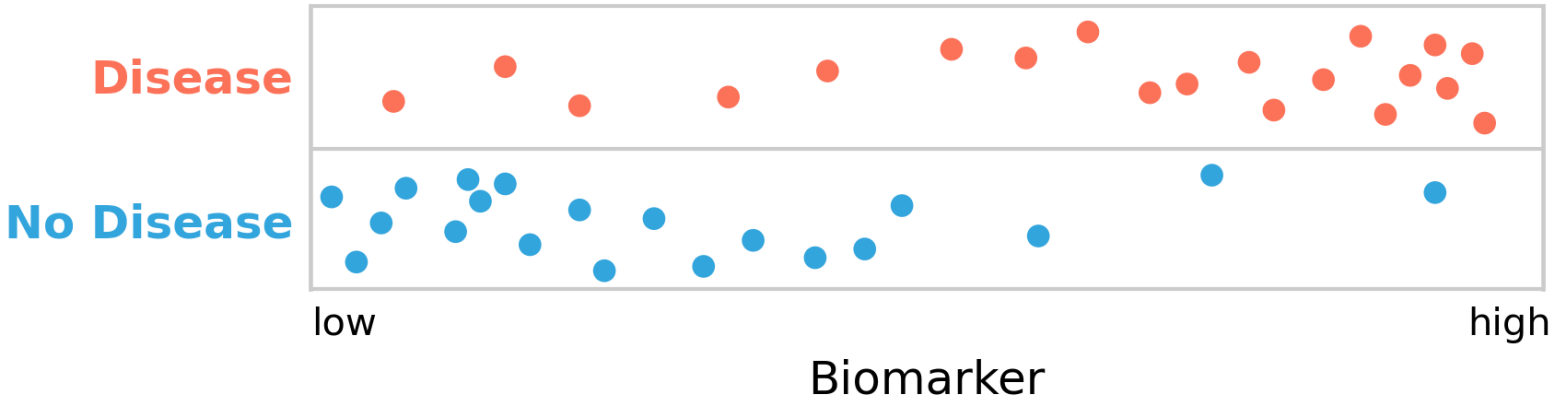
Testing & Diagnostics

2x2

		Test: Positive	Test: Negative
Disease	Present	**True positive**	**False negative**
	Absent	**False positive**	**True negative**

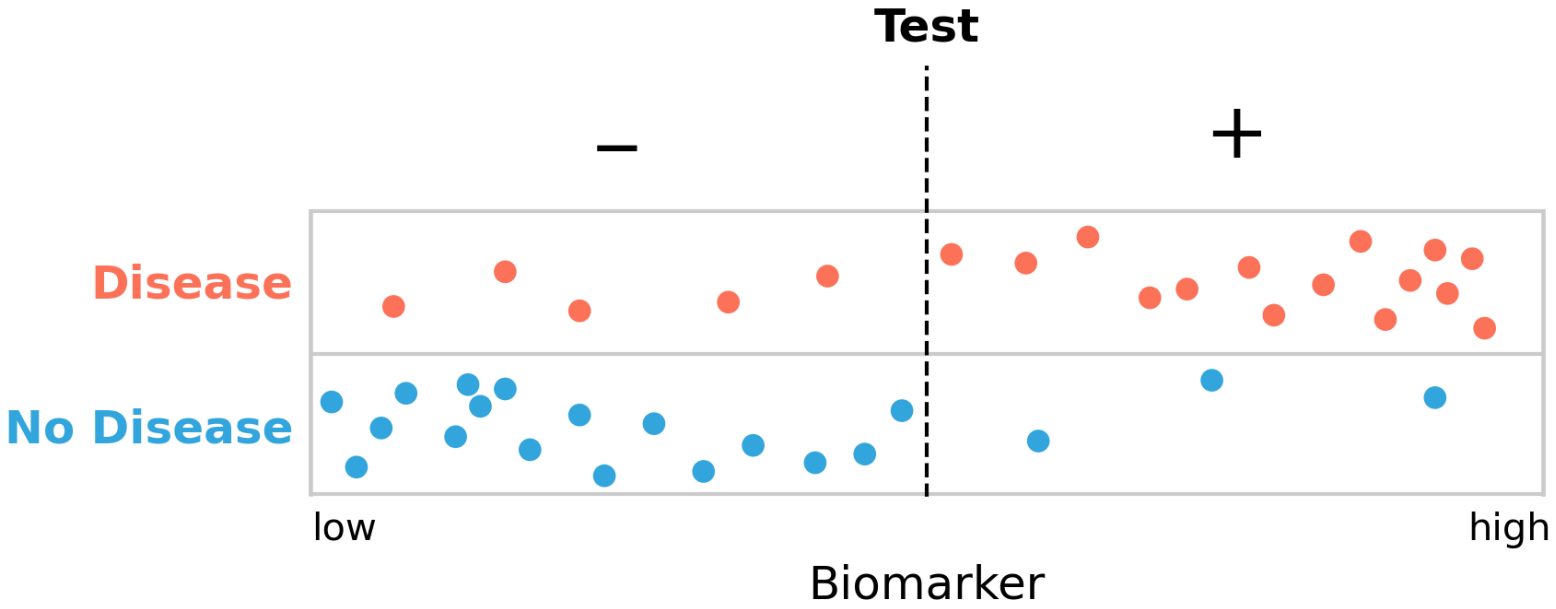
Testing & Diagnostics

Biomarker



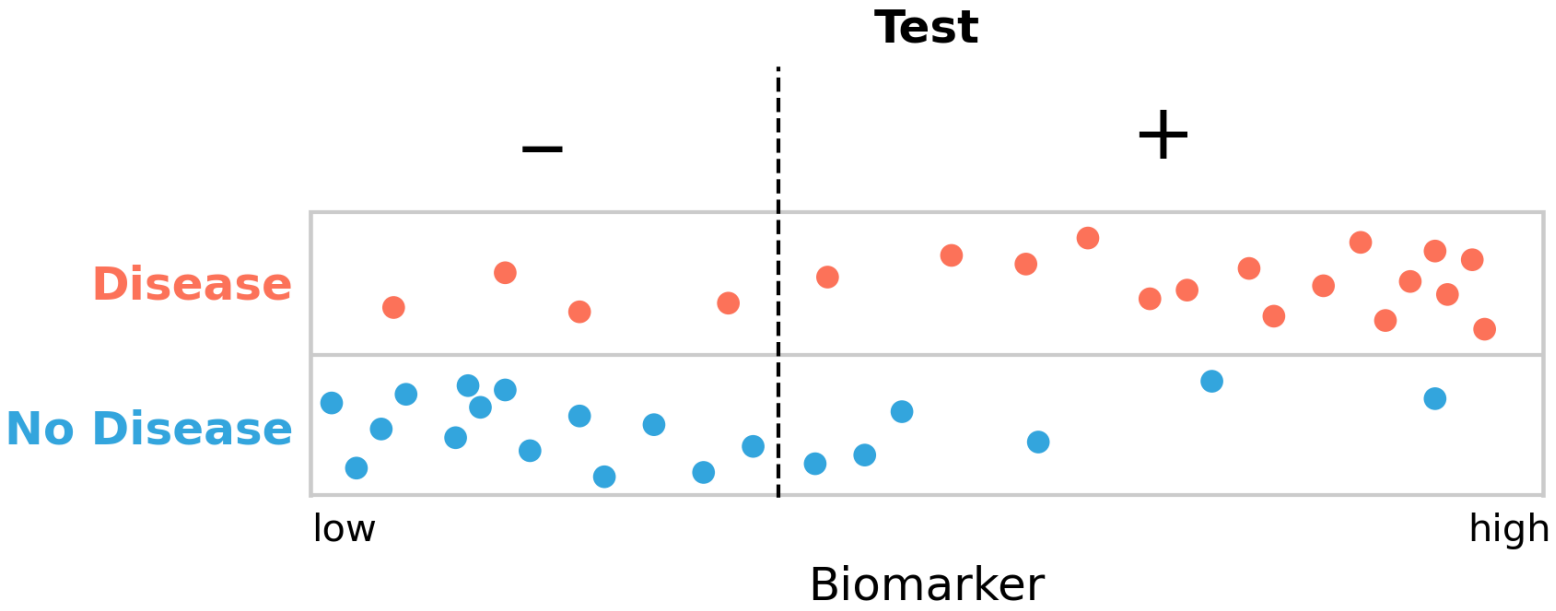
Testing & Diagnostics

Biomarker



Testing & Diagnostics

Biomarker



Testing & Diagnostics
Sensitivity & Specificity

- A sensitive test is a test that rarely misses diseases (few false negatives) - i.e. with small Type II error.
- A specific test is a test that does not misclassify people as diseased when they're not (few false positives) - i.e. with small Type I error.

Testing & Diagnostics
Sensitivity & Specificity

- Sensitivity = $\frac{TP}{TP + FN}$
- Specificity = $\frac{TN}{TN + FP}$

Testing & Diagnostics
Sensitivity & Specificity

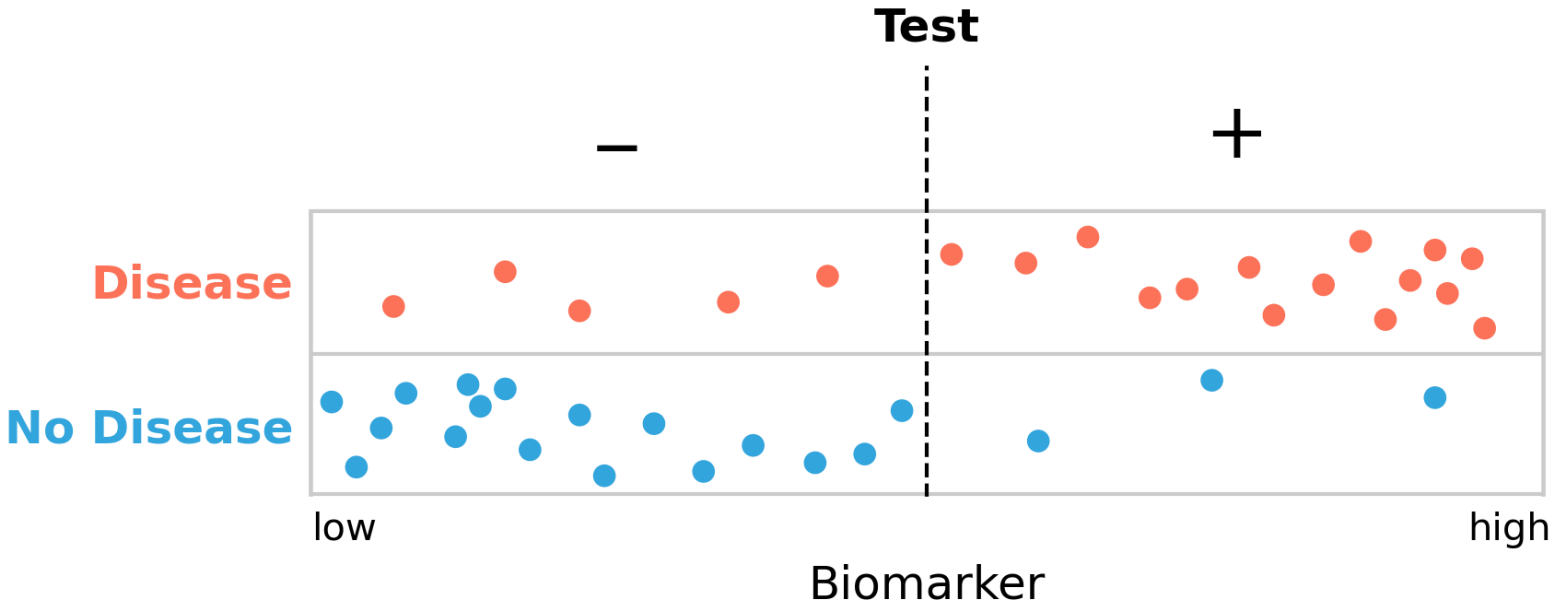
- Sensitivity = $\frac{TP}{TP + FN}$ = True Positive Rate
- Specificity = $\frac{TN}{TN + FP}$ = True Negative Rate

Testing & Diagnostics
Sensitivity & Specificity

- Sensitivity and specificity are both needed to evaluate test!
- Example 1: 100% sensitive test
- Example 2: always positive “test”

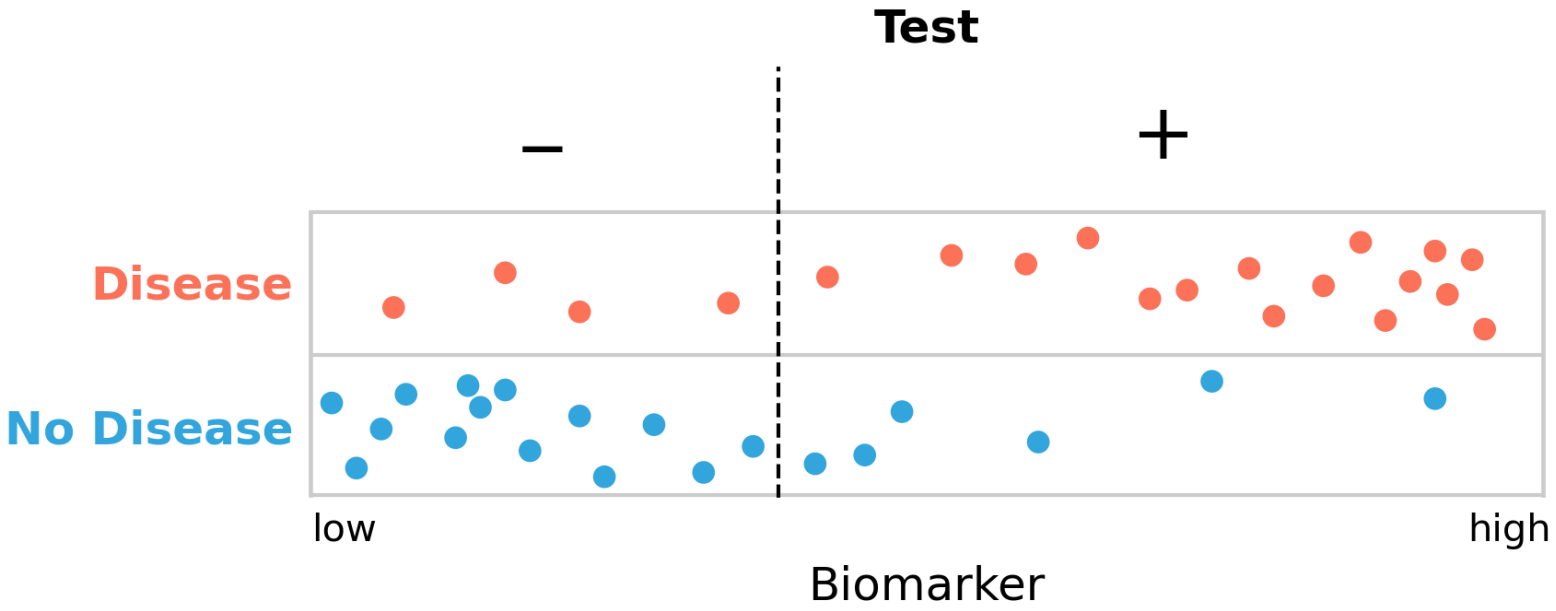
Testing & Diagnostics

Biomarker

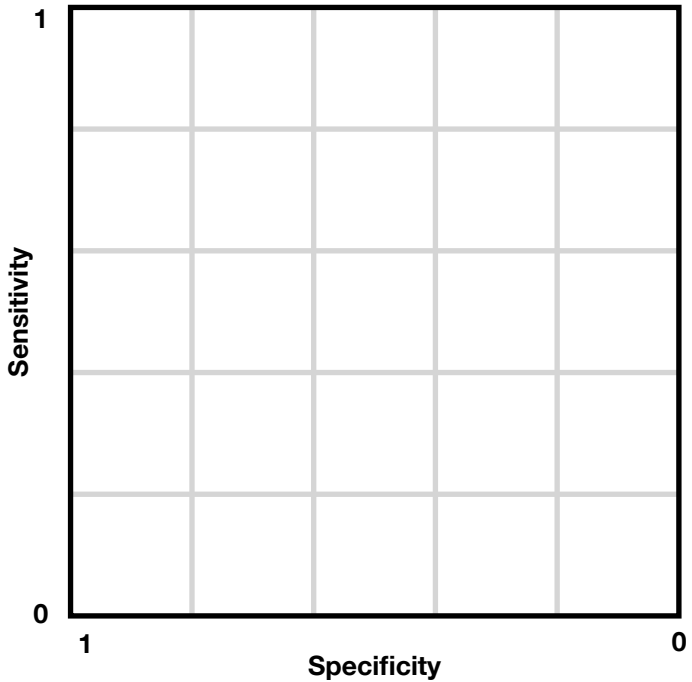


Testing & Diagnostics

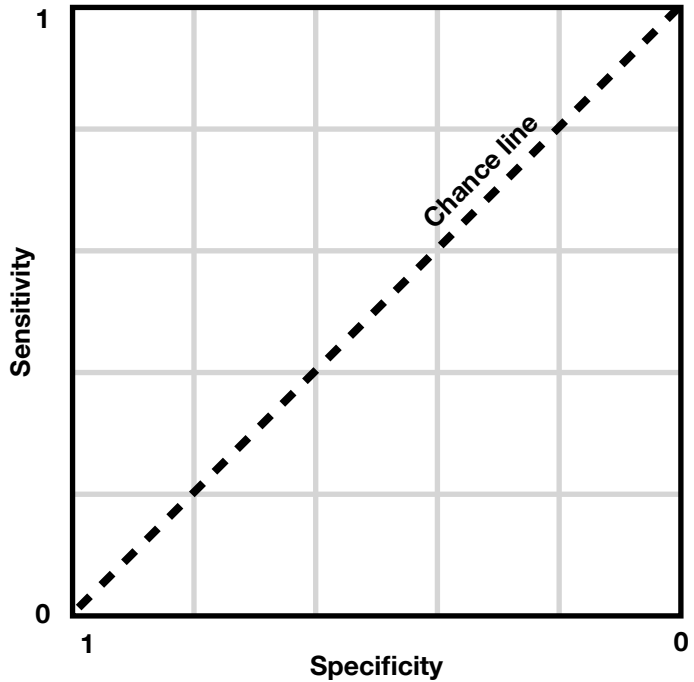
Biomarker



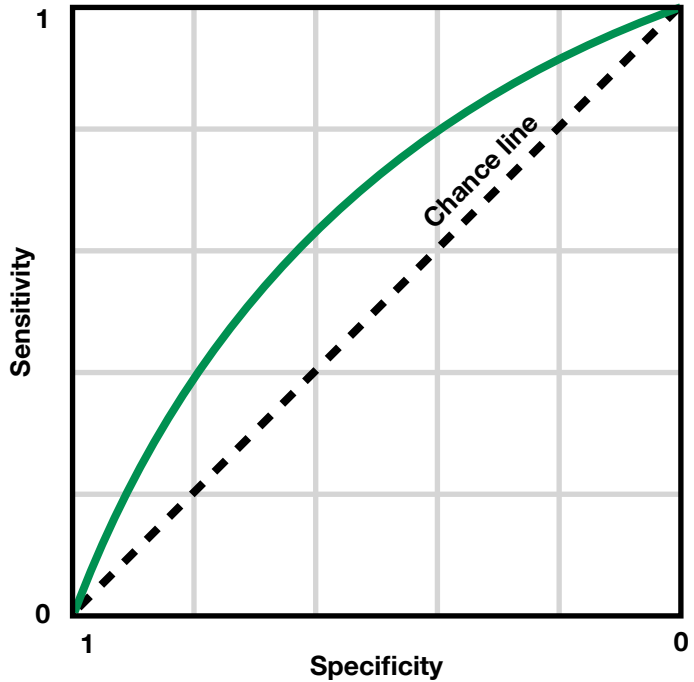
Testing & Diagnostics
ROC Curve



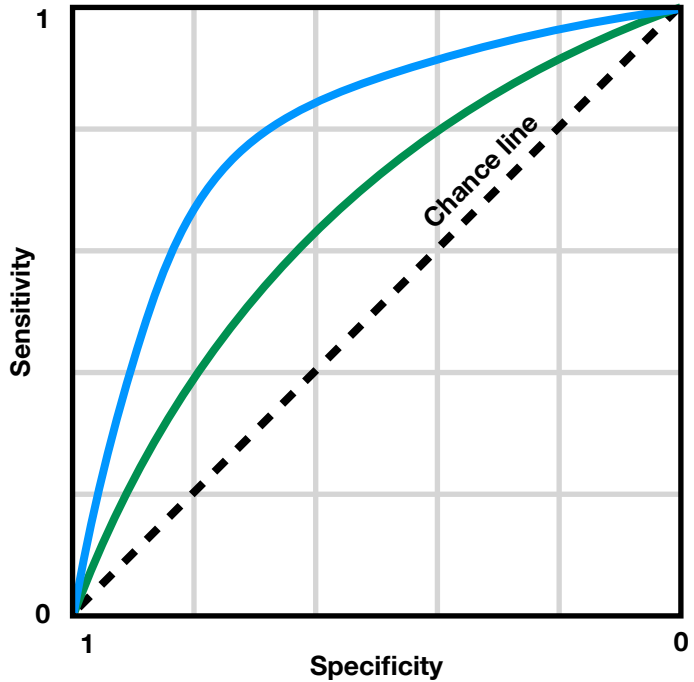
Testing & Diagnostics
ROC Curve



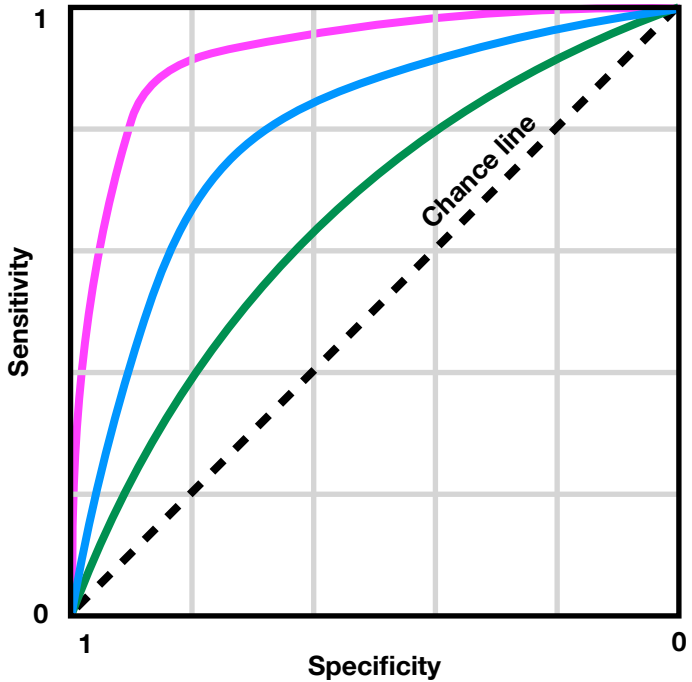
Testing & Diagnostics
ROC Curve



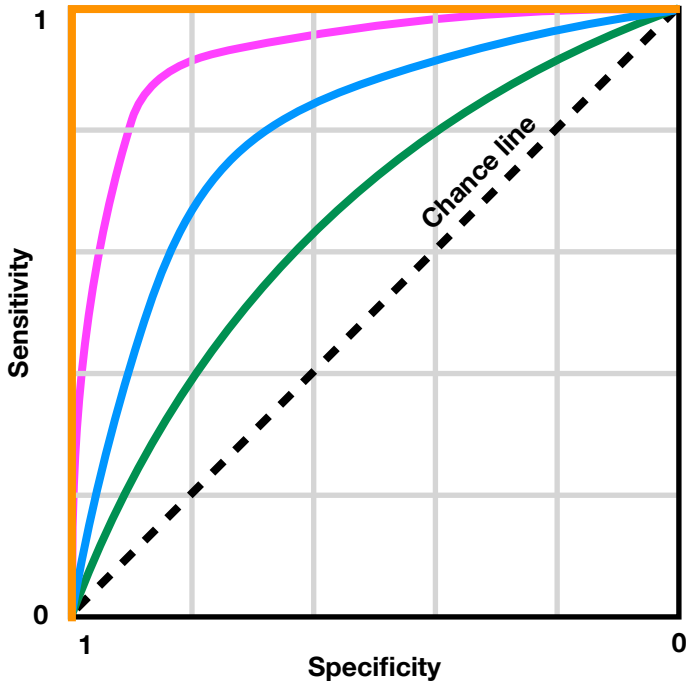
Testing & Diagnostics
ROC Curve



Testing & Diagnostics
ROC Curve

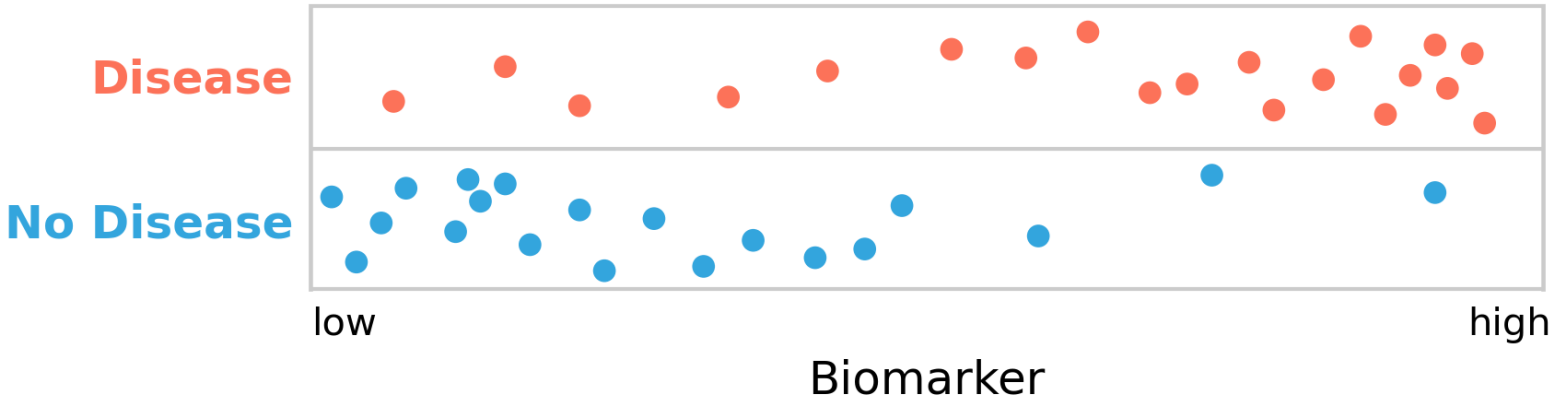


Testing & Diagnostics
ROC Curve



Testing & Diagnostics

Biomarker

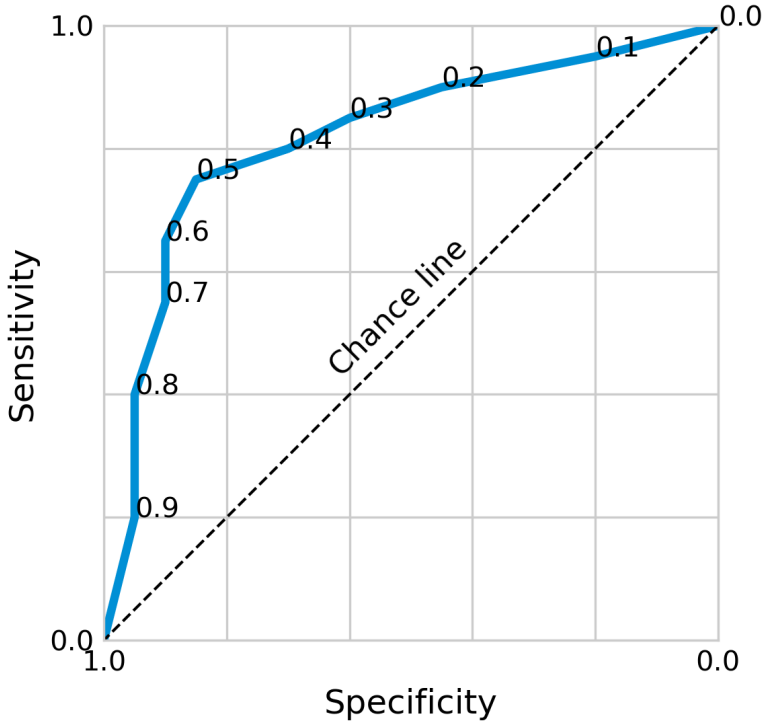


Testing & Diagnostics

Different cutoffs

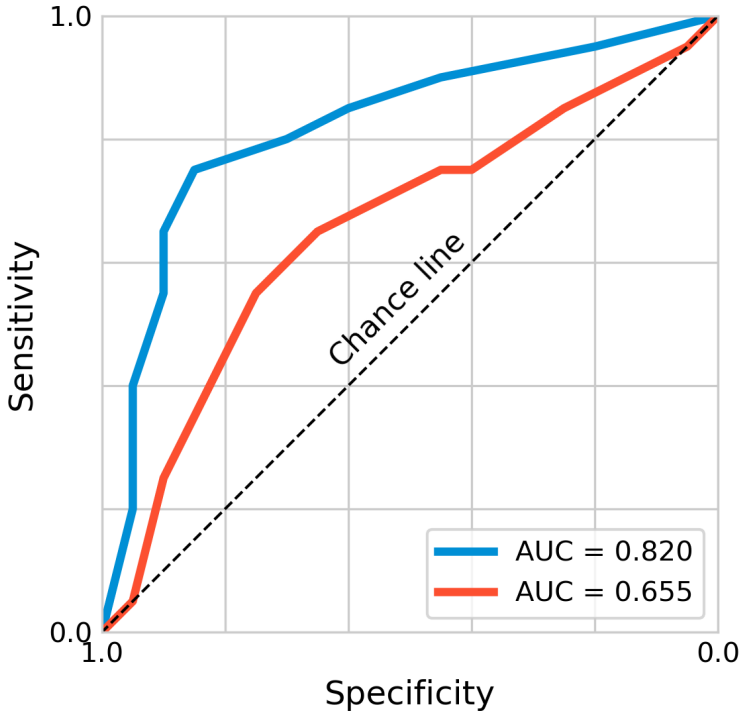
cutoff	sensitivity	specificity
0.1	0.95	0.2
0.2	0.9	0.45
0.3	0.85	0.6
0.4	0.8	0.7
0.5	0.75	0.85
0.6	0.65	0.9
0.7	0.55	0.9
0.8	0.4	0.95
0.9	0.2	0.95

Testing & Diagnostics
ROC Curve



Testing & Diagnostics

ROC Curve



Testing & Diagnostics
Positive predictive value

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Large-Scale Assessment of a Smartwatch to Identify Atrial Fibrillation

Marco V. Perez, M.D., Kenneth W. Mahaffey, M.D., Haley Hedlin, Ph.D., John S. Rumsfeld, M.D., Ph.D., Ariadna Garcia, M.S., Todd Ferris, M.D., Vidhya Balasubramanian, M.S., Andrea M. Russo, M.D., Amol Rajmane, M.D., Lauren Cheung, M.D., Grace Hung, M.S., Justin Lee, M.P.H., Peter Kowey, M.D., Nisha Talati, M.B.A., Divya Nag, Santosh E. Gummidipundi, M.S., Alexis Beatty, M.D., M.A.S., Mellanie True Hills, B.S., Sumbul Desai, M.D., Christopher B. Granger, M.D., Manisha Desai, Ph.D., and Mintu P. Turakhia, M.D., M.A.S., for the Apple Heart Study Investigators*

ABSTRACT

BACKGROUND

Optical sensors on wearable devices can detect irregular pulses. The ability of a smartwatch application (app) to identify atrial fibrillation during typical use is unknown.

From the Division of Cardiovascular Medicine (M.V.P.), Stanford Center for Clinical Research (K.W.M., A.R., N.T.),

Testing & Diagnostics

Positive predictive value

RESULTS

We recruited 419,297 participants over 8 months. Over a median of 117 days of monitoring, 2161 participants (0.52%) received notifications of irregular pulse. Among the 450 participants who returned ECG patches containing data that could be analyzed — which had been applied, on average, 13 days after notification — atrial fibrillation was present in 34% (97.5% confidence interval [CI], 29 to 39) overall and in 35% (97.5% CI, 27 to 43) of participants 65 years of age or older. Among participants who were notified of an irregular pulse, the positive predictive value was 0.84 (95% CI, 0.76 to 0.92) for observing atrial fibrillation on the ECG simultaneously with a subsequent irregular pulse notification and 0.71 (97.5% CI, 0.69 to 0.74) for observing atrial fibrillation on the ECG simultaneously with a subsequent irregular tachogram. Of 1376 notified participants who returned a 90-day survey, 57% contacted health care providers outside the study. There were no reports of serious app-related adverse events.

Testing & Diagnostics
Positive predictive value

- Imagine you are getting diagnosed with a positive test. What is the probability that you actually have the disease?

- Initial intuition: depends on accuracy of test

Testing & Diagnostics

Positive predictive value

- Example:
  - Test sensitivity: 92%
  - Test specificity: 91%
  - Disease prevalence: 0.9%

Testing & Diagnostics
Positive predictive value

- Disease prevalence is essential. Careful: which population are we looking at?

- E.g. Cancer prevalence in general population < Cancer prevalence in a high risk population.

Testing & Diagnostics

Bayes' Theorem

$$P(A|B) = \frac{P(B|A)\,P(A)}{P(B)}$$

Testing & Diagnostics

Bayes' Theorem

$$P(D|T+) = \frac{P(T+|D)\,P(D)}{P(T+)}$$

Testing & Diagnostics

Bayes' Theorem

$$P(D|T+) = \frac{P(T+|D)\,P(D)}{P(T+|D)P(D) + P(T+|\neg D)P(\neg D)}$$

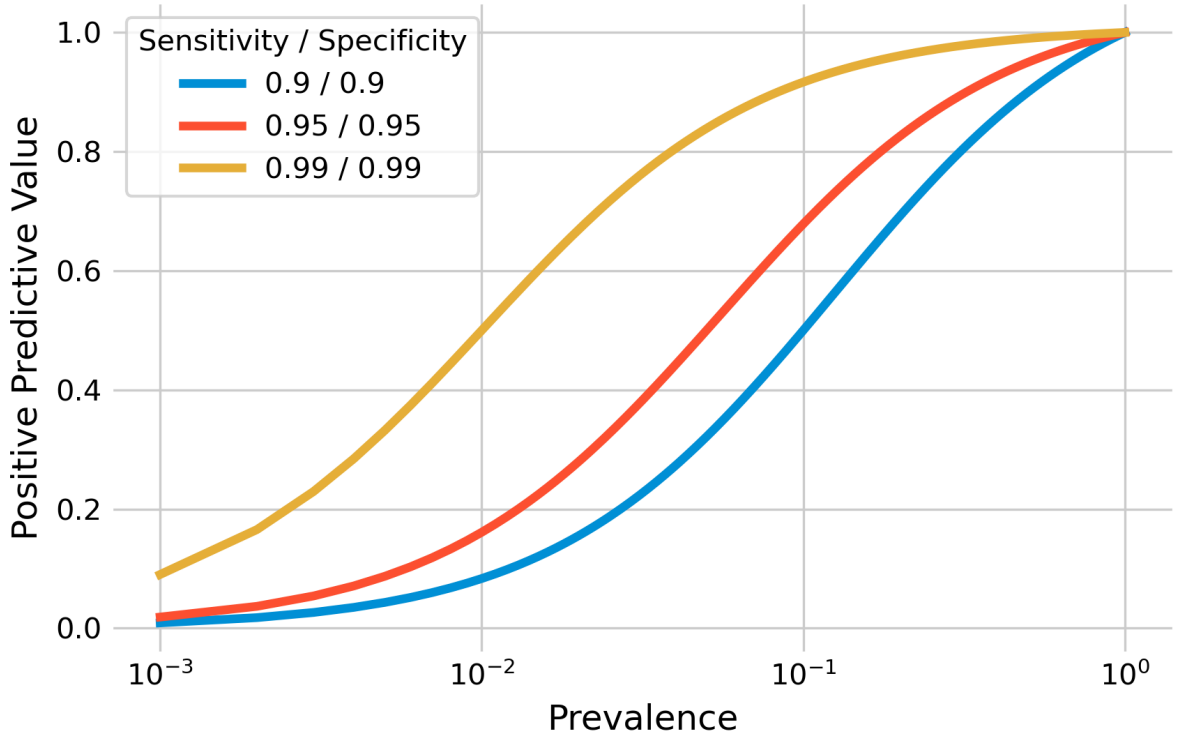
Testing & Diagnostics

Positive predictive value

$$\frac{sensitivity * prevalence}{sensitivity * prevalence + (1 - specificity) * (1 - prevalence)}$$

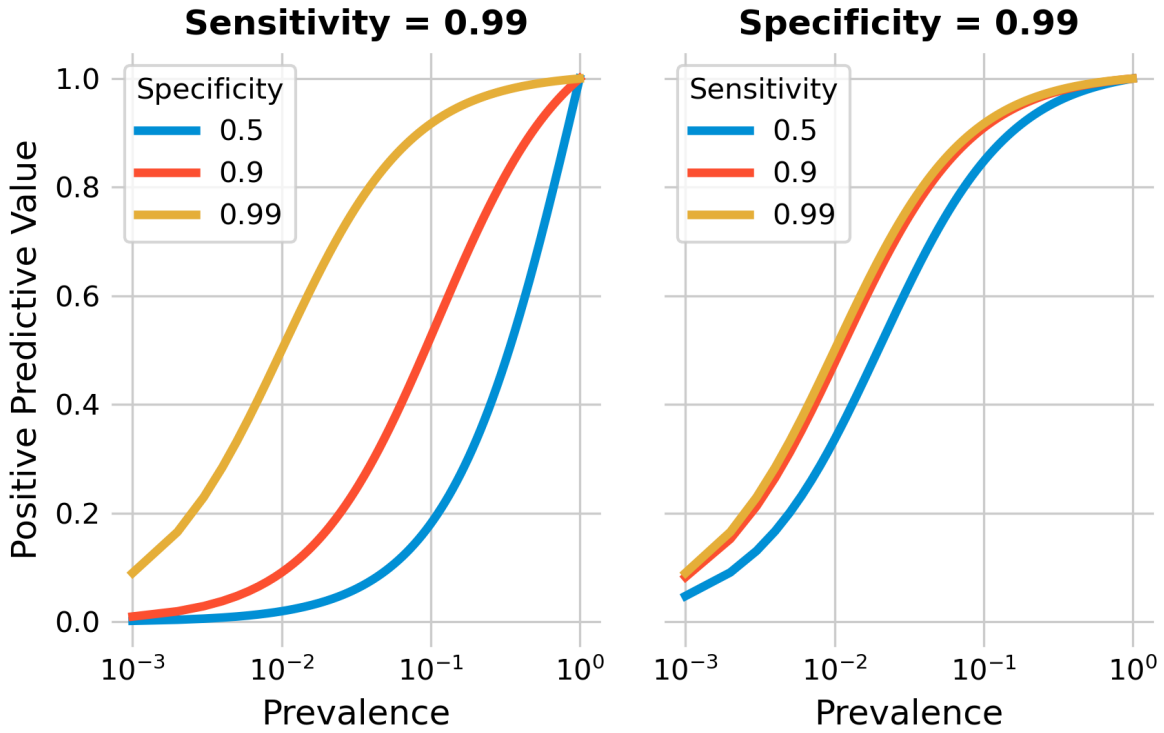
Testing & Diagnostics

Positive predictive value



Testing & Diagnostics

Positive predictive value




THE DAILY SHOW
WITH TREVOR NOAH
PROBLEM SOLVED.

Testing & Diagnostics
Likelihood ratios

- Prevalence = pre-test probability of having disease
- Positive predictive value = post-test probability of having disease

It would be nice to transform one into the other!

Testing & Diagnostics

Likelihood ratios

$$LR+ = \frac{P(T+|D)}{P(T+|\neg D)}$$

Testing & Diagnostics
Likelihood ratios

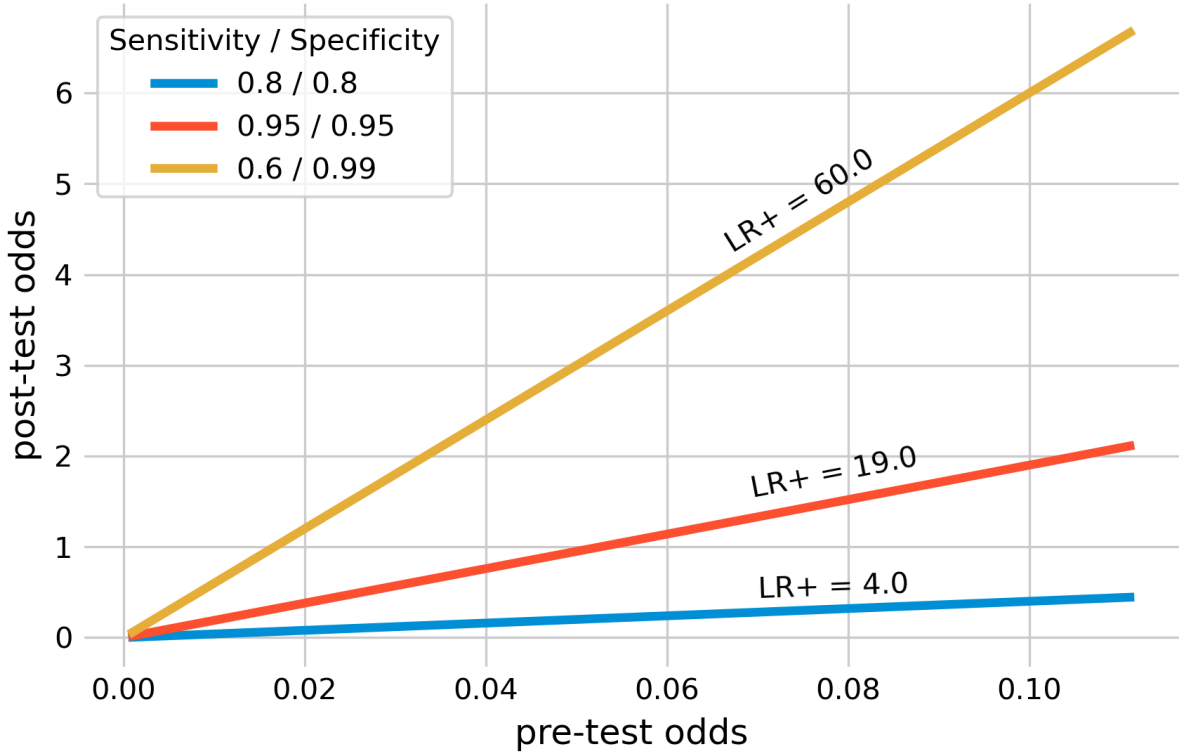
- Likelihood ratios work most easily with odds, not probabilities

Testing & Diagnostics
Likelihood ratios

- post-test odds = LR * pre-test odds

Testing & Diagnostics

Likelihood ratios



Testing & Diagnostics

Rule in, rule out

- “SpPIn, SnNOut”, which stands for “**sp**ecific, **p**ositive, rule **in**” and “**s**e**n**sitive, **n**egative, rule **out**